Citizen Petitions: Long, Late-Filed, and At-Last Denied

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ABSTRACT

The pharmaceutical industry is ground zero for many of the most challenging issues at the intersection of antitrust and intellectual property (IP) law. It also presents a complex regulatory regime that is ripe for anticompetitive behavior. It thus should not be a surprise that the industry has been subject to rigorous antitrust scrutiny in recent years.

While settlements between brand and generic firms and "product hopping" from one version of a drug to another have received attention, one behavior has avoided serious scrutiny. Brand firms' filing of citizen petitions with the U.S. Food and Drug Administration (FDA) has almost entirely slipped beneath the radar. While citizen petitions in theory could raise concerns that a drug is unsafe, in practice they bear a dangerous potential to extend brand monopolies by delaying approval of generics, at a potential cost of millions of dollars per day.

This Article offers an empirical study of "505(q)" citizen petitions, which ask the FDA to take specific action against a pending generic application. It analyzes every 505(q) petition filed with the FDA between 2011 and 2015, documenting (1) the number of petitions each year, (2) who files the petitions, (3) the success rate of the petitions, (4) the petitions' length, (5) whether petitions were filed in close proximity to the expiration of a patent or data exclusivity date, and (6) occasions in which the FDA approved generics on the same day it decided petitions.

The study finds that brand firms file 92% of 505(q) petitions. And it concludes that the FDA grants an astonishingly low 8% of petitions, rejecting a full 92%. Why is the grant rate so low? We consider several reasons. First, in the past 5 years, the average length of petitions has more than doubled, and the FDA almost never grants petitions with a length above the mean. Second, 39% of petitions are filed within 6 months of the expiration of a patent or FDA exclusivity date, with almost all of these petitions denied. Third, the FDA resolved a number of petitions on the same day it approved the generic, likely delaying generic entry. These three settings result in grants of only 3%, 2%, and 0%, respectively.

The Article concludes by offering examples of serial petitions, late-filed petitions, and a combination of petitions with other behavior such as product-hopping and settlements. In short, citizen petitions represent a hidden tool in brands' toolkit of entry-delaying activity, and when used inappropriately force consumers to pay high drug prices while providing no offsetting safety benefit.

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INTRODUCTION

The pharmaceutical industry is ground zero for many of the most challenging issues at the intersection of antitrust and intellectual property (IP) law. Patents play a crucial role in the development of drugs, which is costly and takes years to reach the market. But the complexity of the regulatory regime and the dramatic effects on brand profits when generics enter the market provide a setting rife with potentially anticompetitive behavior.

It thus should not be a surprise that the industry has been subject to rigorous antitrust scrutiny in recent years. Courts have

examined "pay for delay" settlements by which brand-name drug companies pay generics to settle patent litigation and delay entering the market. Courts also have scrutinized "product hopping," by which a brand firm switches from one version of a drug to another, often for the sole purpose of delaying generic entry.

Amidst all this attention, one behavior has avoided serious scrutiny. Brand firms' filing of citizen petitions with the U.S. Food and Drug Administration ("FDA") has almost entirely slipped beneath the radar. In theory, citizen petitions could raise concerns that a drug is unsafe. But in practice they bear a dangerous potential to extend brand monopolies by delaying approval of generics, at a potential cost of millions of dollars *per day*.

Not all citizen petitions raise anticompetitive concern. But one type is potentially troublesome: the so-called "505(q)" petition. These are petitions that ask the FDA to take a particular action against a pending generic application. In fact, Congress specifically addressed these petitions when it passed a law requiring the FDA to resolve them in an expedient manner to avoid generic delay.

This Article offers an empirical study of every 505(q) citizen petition filed with the FDA between 2011 and 2015. It documents (1) the number of petitions filed each year, (2) who files the petitions, (3) the success rate of the petitions, (4) the petitions' length, (5) whether petitions were filed immediately before patent or data expiration dates, and (6) whether the FDA approved generics on the same day (or in the same month) it decided the citizen petition.

The study finds that brand firms file 92% of 505(q) petitions—each attacking a proposed generic. And remarkably, the FDA has granted *only 8%* of petitions, while denying 92%. In other words—and based on the first empirical survey of citizen petitions we conducted several years ago—the already low rate of 19% of petitions granted from 2001 to 2010 fell by more than half in the succeeding 5 years. In short, 505(q) citizen petitions are almost never granted.

Why is the grant rate so low? We explore several reasons. First, in the past 5 years, the length of petitions has more than doubled. The FDA grants only 3% of petitions with a length above the mean, supporting the thesis that they are filed to hamstring the FDA and delay generic entry rather than raise legitimate safety

concerns.

Second, 39% of the brand products protected by 505(q) petitions witness a petition filed within 6 months of the expiration of a patent or FDA exclusivity date. Here as well, almost none of the petitions (2%) are granted. And third, the FDA granted approval to 6 generics on the same day (and an additional 17 in the same month) it resolved a petition, denying every one of the petitions and raising the concern that the FDA is delaying generic approval until it dispenses with the citizen petition.

We conclude by offering examples of concerning petitions. COPAXONE® presents an instance of serial petitions, with Teva filing *eight* petitions to delay a generic version of the multiple-sclerosis drug. Late-filed petitions also raise questions, such as when Bayer Healthcare filed a petition *one day* before the expiration of the patent on MIRENA®, a long-acting intrauterine device (IUD). The combination of citizen petitions and other behavior such as product-hopping raises concern, as shown by the example of acne-treating DORYX®. And Mylan's allergic-emergency-treating EpiPen® reveals the combination of petitions and settlements.

Part I of this Article introduces the Hatch-Waxman Act, enacted by Congress in 1984 to create a framework for brand and generic pharmaceutical competition. It also discusses brand-generic settlements as well as product hopping. Part I pays particular attention to the importance of generic competition and timing of generic entry.

Part II turns to citizen petitions, providing an introduction to the conduct and showing how they are filed most frequently in the pharmaceutical industry. The Part focuses on 505(q) petitions, which ask the FDA to take specific action against a pending generic application and which arose out of 2007 legislation designed to prevent generic delay.

After presenting our methodology, Part III analyzes 505(q) petitions, as well as the grant/denial rate in general and for brand petitions in particular. Part IV then explores some reasons for low success rates. It traces the increasing complexity of petitions, the number of brand products witnessing a petition filed within 6 months of the expiration of a patent or FDA exclusivity, and the number of petitions the FDA resolved on the same day (or in the

same month) it approved a generic. For each of these cases, it compares the grant/denial rates to the overall figures.

Finally, Part V offers examples of concerning behavior based on serial petitions, late-filed petitions, and the combination of citizen petitions with product hopping and settlements. In short, citizen petitions represent a hidden tool in brands' toolkit of entry-delaying activity, and when used inappropriately force consumers to pay high drug prices while providing no offsetting safety benefit.

I. PHARMACEUTICAL COMPETITION

The pharmaceutical industry presents challenging issues lying at the intersection of intellectual property, antitrust, and regulatory law.[1]

A. Hatch-Waxman Act

The regulatory structure governing the pharmaceutical industry is the Hatch-Waxman Act, which Congress enacted in 1984 to increase generic competition and foster innovation.[2] Generic drugs have the same active ingredients, dosage, administration, performance, and safety as patented brand drugs.[3] But despite the equivalence, generic manufacturers were required, at the time of the Hatch-Waxman Act, to engage in lengthy and expensive trials to demonstrate safety and effectiveness.[4] The FDA approval process

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[1] Portions of this section are adapted from Michael A. Carrier & Daryl Wander, *Citizen Petitions: An Empirical Study*, 34 CARDOZO L. REV. 249 (2012).

[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). 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).

[3] *Understanding Generic Drugs*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm (last updated Apr. 14, 2016).

[4] Before the enactment of the Act, some generic firms were able to file "paper NDAs," use the antiquated Abbreviated New Drug Application

took several years, and because the required tests constituted infringement of the brand firm's patent covering the drug, generics could not begin the process during the patent term.[5] They therefore waited until the end of the term to begin these activities, which prevented them from entering the market until two or three years after the patent expired. At the time Congress enacted Hatch-Waxman, there were no generic equivalents for roughly 150 drugs whose patent term had lapsed.[6]

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

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system, or use the monograph system established for generic antibiotics and insulin to avoid conducting their own clinical trials. Edward Tabor, *Generic Drug Approvals in the U.S. prior to the Hatch-Waxman Act*, REG. FOCUS, at 50 (Sept. 2008).

[5] CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 38 (1998), *available at* https://www.cbo.gov/publication/10938?index=655 [hereinafter CBO STUDY].

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

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

[8] FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 5 (2002), *available at* https://www.ftc.gov/os/2002/07/genericdrugstudy.pdf. A previous application process with the same name had existed in the regulations as early as 1969, but this previous ANDA bears little resemblance to the ANDA process established by the Hatch-Waxman Act. 34 Fed. Reg. 2673 (Feb. 27, 1969) (discussing creation of previous ANDA).

patent.[9]

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,[10] increased to 80% as of 2014.[11] For the most popular drugs with expired patents, the share facing generic competition burgeoned from 35% in 1983 to almost 100% today.[12]

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.[13] The presence of a second generic lowers the price to approximately half the brand price.[14] In markets in which six or more generics enter, the price falls to a quarter of the brand price.[15] One survey showed that patients could save 52% in the daily costs of their medications by purchasing generic drugs.[16] In fact, even

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[9] 21 U.S.C. § 355(j)(5)(B)(iv).

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

[11] GPhA, *Generic Drug Savings in the U.S.: Seventh Annual Edition: 2015*, *available at* http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf.

[12] CBO STUDY, *supra* note 5, at 37.

[13] *Id.* at xiii; *Generic Competition and Drug Prices*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm (last updated May 13, 2015).

[14] *Id.*

[15] *Id.*

[16] *Savings From Generic Drugs Purchased at Retail Pharmacies*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm134205.htm (last updated May 6, 2016).

though generics make up 80% of prescriptions, they amount to only 28% of drug costs.[17]

In addition, generic drugs quickly take sales from brand drugs. Once a generic enters the market, a brand loses 45% to 90% of its market share within the first twelve months.[18] Generic entry is most likely for drugs with large markets, particularly those with blockbuster products, but occurs with respect to drugs in markets of many sizes.[19]

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

For these reasons, it is in brand firms' interests to delay generic entry. Every day a brand firm can control the market and forestall entry is a day it could gain monopoly profits. In the Hatch-Waxman setting, this is particularly tempting since brands could face generic entry before the end of the patent term.

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[17] GPhA, *Generic Drug Savings*, *supra* note 11, at 1.

[18] FED. TRADE COMM'N, PAY-FOR-DELAY: HOW DRUG COMPANY PAYOFFS COST CONSUMERS MILLIONS 8 (2010), *available at* http://www.ftc.gov/os/2010/01/100112payfordelayrpt.pdf; CBO STUDY, *supra* note 5, at xiii; DOUG LONG, IMS HEALTH, 2003 YEAR IN REVIEW: TRENDS, ISSUES, FORECASTS 35 (2004), *available at* http://www.piapr.org/index.php?src=documents&srctype=download&id=38; Atanu Saha et al., *Generic Competition in the U.S. Pharmaceutical Industry*, 13 INT'L J. ECON. BUS. 15, 31 (2006).

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

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

[21] *Id.* at 23–24.

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

C. Conduct Delaying Generic Entry

Because of the dramatic effects of generic competition, brand firms have used an array of tactics to delay entry. One activity involves patent litigation settlements in which brands pay generics to settle their lawsuit and refrain from entering the market. While many of these settlements do not raise concern because the parties reach an "entry-date" agreement reflecting the strength of the patent, some do not. In particular, brand firms have paid generics to delay entering the market, a practice the Supreme Court held could have "significant adverse effects on competition" and violate the antitrust laws.[23] If a brand is able to prevent a generic from challenging a patent and entering the market, it can block not only that company, but also all other generics, from entering.[24] Paying a company that seeks to invalidate a patent on a drug can delay significant generic penetration for an extended period of time.

Another activity that has raised the concern of delayed generic entry is "product hopping," which refers to a brand'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.[25] Much of this product-hopping activity has been successful because it has avoided the effect of state drug product substitution ("DPS") laws,[26] in effect in all 50 states today, which allow (and sometimes require) pharmacists—absent a doctor's contrary instructions—to substitute generic versions of brand-name prescriptions.[27] These laws, however, can be evaded when brand firms engage in product hopping prior to generic entry. Switching patients to a new version of the drug before generic entry prevents a pharmacist from substituting a generic version because

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[23] FTC v. Actavis, 133 S. Ct. 2223, 2231 (2013).

[24] *See* Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV. 7, 15 (2014).

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

[26] *See id.* at 13–18.

[27] *See* Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1017 (2010).

the generic is not equivalent to the new brand version.[28]

A central issue in both settlements and product hopping involves timing. Product hopping is most successful when brand firms not only can avoid state DPS laws but also can switch the market before generic entry. Brands 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.[29] Patients who switch to the new drug are unlikely to switch back.[30]

Firms have employed a combination of settlements and product hopping to ensure that they can switch to a new version before generics enter the market on the old version. The value of the conduct in combination is that a settlement that prevents patent challenges for a period of time—even if less than the duration of the patent—allows the brand to switch the market to the new product. So by the time, years later, that the generic enters, the market will have already migrated to the new product. As a result, the generic, which can no longer take advantage of state DPS laws, fails to provide meaningful downward pressure on the brand's new drug price.

Brands' use of citizen petitions could be a valuable addition to this strategy. By requesting that the FDA make a decision on safety and efficacy—often by reviewing a wealth of material and studies—brands could buy additional time in which to delay generic entry. This Article focuses on citizen petitions, presenting original data that shows how they are used as a part of brands' delay strategy.

II. CITIZEN PETITIONS: OVERVIEW

This Part provides a background on citizen petitions and explores the industries in which they are filed and the various types of petitions. It then discusses congressional reports on the topic before presenting the findings of our previous study on the conduct.

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[28] Leffler et al., *supra* note 25, at 5.

[29] *Id.* at 51.

[30] *Id.* at 51–55.

A. Introduction

The First Amendment ensures that Congress cannot abridge "the right of the people . . . to petition the Government" to take a particular action.[31] 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.[32] The FDA allows individuals to express safety, scientific, or legal issues in such a petition regarding a product.[33]

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."[34]

All citizen petitions must include the "action requested," particularly the "rule, order, or other administrative action" that the petitioner seeks to "issue, amend or revoke."[35] Petitions also must disclose a "[s]tatement of grounds," including "the factual and legal grounds for the petition."[36]

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[31] U.S. CONST. amend. I ("Congress shall make no law . . . abridging the freedom . . . to petition the Government for a redress of grievances."). This and the following 3 paragraphs are adapted from Carrier & Wander, *supra* note 1, at 259-60.

[32] 5 U.S.C. § 553(e); *see also* Stacey B. Lee, *Is a Cure on the Way?*, 20 KAN. J.L. & PUB. POL'Y 98, 108–09 (2010).

[33] 21 C.F.R. § 10.30(a) (2012); *The Generic Drug Maze: Speeding Access to Affordable, Life-Saving Drugs: Hearing Before the S. Spec. Comm. on Aging*, 109th Cong. 6 (2006) [hereinafter *Generic Drug Maze Hearing*], *available at* http://aging.senate.gov/publications/7202006.pdf (statement of Gary Buehler, Director, Office of Generic Drugs, Food & Drug Admin.); *see also* 21 C.F.R. § 10.30(b)(B) (requiring petitions to state factual and legal grounds for requests).

[34] 21 C.F.R. §§ 10.25, 10.30.

[35] 21 C.F.R. § 10.30(b)(A); *Comment on Proposed Regulations and Submit Petitions*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/AboutFDA/ContactFDA/CommentonRegulations/default.htm (last updated Oct. 20, 2014).

[36] 21 C.F.R. § 10.30(b)(B).

Citizen petitions additionally must describe any environmental effects of the requested action.[37] 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."[38]

Citizen petitions may raise valid safety concerns, but in many cases, they offer little incremental value and the FDA is forced to spend considerable time responding to them. The agency is required to address the merits of every citizen petition submitted, many of which contain "detailed analysis and precise scientific documentation" and require review by "multiple disciplines within [the FDA's Center for Drug Evaluation and Research (CDER)],"[39] which has led to a backlog at the FDA.

The FDA's jurisdiction covers many industries. Table 1 shows, though, that the vast majority of citizen petitions concern drugs. And even though the number of petitions targeting drugs decreased from 75% in 2013 to 65% in 2015, the industry still provides the setting for an overwhelming share of petitions. Far behind, but with multiple petitions, are the food and medical device industries.

Table 1
Citizen Petitions by Industry[40]

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[37] *Id.* § 10.30(b)(C).

[38] *Id.* § 10.30(b)(D).

[39] *The Generic Drug Maze: Speeding Access to Affordable, Life-Saving Drugs: Hearing Before the S. Spec. Comm. on Aging*, 109th Cong. 14 (2006) (statement of Gary Buehler, Director, Office of Generic Drugs, Food & Drug Admin.).

[40] As noted below, see *infra* Section III.A, the FDALawBlog's Citizen Petition Tracker began tracking all types of petitions in 2013. Before 2013, the Tracker listed only 505(q) petitions (which by definition occur with respect to drugs), which explains why we do not present data from 2011 and 2012 in Tables 1 and 2.

	2013	2014	2015
Animal Drugs	8	4	1
Biologics	3	3	3
Cosmetics	0	0	3
Device	3	0	3
Dietary Supplements	2	1	2
Drug	131	117	92
Drug/Medical Device	1	0	1
Drug/Dietary Supplement	0	1	0
Food	7	16	13
Food, Dietary Supplement, and Drugs	1	0	0
Medical Device	14	18	15
Other	0	1	1
Tobacco	4	0	1
Total	174	161	142
% Drug Petitions	75%	73%	65%

Actors in the pharmaceutical industry have filed various

petitions that can be subdivided into five different types: general citizen petitions, reference listed drug (RLD) designation petitions, discontinuation petitions, ANDA suitability petitions, and 505(q) certified petitions. Table 2 provides a breakdown of these different types.

Table 2
Types of Drug Petitions

	2013	2014	2015
Citizen Petition	42	39	26
505(q) Certification	37	25	17
RLD	12	14	18
Discontinuation	21	13	12
ANDA Suitability	21	27	16
Discontinuation/ANDA Suitability	0	0	1
RLD/Discontinuation	0	1	0
Advisory Opinion	0	0	1
Petition for Stay of Action	3	0	0

General citizen petitions raise issues related to safety or industry guidelines and are filed by various actors in the pharmaceutical and biotechnology fields, including drug companies, universities, doctors, and public interest groups.[41]

[41] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-1900 (filed on May 27, 2015) (petition submitted by CUNY School of Public Health and Hunter

RLD designation petitions ask that the FDA designate a particular approved drug as a reference listed drug for the purposes of filing an ANDA.[42]

Discontinuation petitions require that the FDA confirm whether an approved drug product was taken off the market for safety or efficacy concerns.[43]

ANDA suitability petitions ask that the FDA confirm whether a prospective generic application can consist of certain features.[44]

505(q) citizen petitions, the focus of this Article, ask the FDA to take a particular action against a pending generic application and are the petitions brands are most likely to file to delay generic entry.

Section 505(q) appeared in Section 914 of Title IX of the Food and Drug Administration Amendments Act ("FDAAA") of 2007.[45] Congress intended to reduce delays from petitions,[46] with Section 505(q) applying to "certain petitions that request that FDA take any form of action related to a pending ANDA" and requiring petitioners to certify that they did not delay in filing the petition.[47] The FDAAA mandated that the FDA take final action no later than

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College, requesting that FDA mandate certain label language for contraception product).

[42] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-1899 (filed on May 27, 2015).

[43] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-1752 (filed on May 15, 2015).

[44] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-1590 (filed on May 6, 2015) (requesting FDA permission to file ANDAs on 10 mg/vial and 30 mg/vial for new strength formulations while referencing 60 mg/vial brand drug).

[45] 21 U.S.C. § 355(q).

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

[47] *See* 153 CONG. REC. 25,047 (2007).

180 days (later shortened to 150 days[48]) after the petition's filing date unless delay would be necessary to protect the public health.

As shown below,[49] brand firms have filed the vast majority of 505(q) petitions. These brand petitions have largely sought to require the generic to perform additional testing before entering the market. And they have questioned whether generics are bioequivalent, in other words, able to deliver the same amount of active ingredient to the site of action with the same rate and extent of absorption into the body.

Generics also have filed 505(q) petitions. In one scenario, they have sought to mandate certain types of bioequivalence testing on other generic applications.[50] In another, first-filing generics have requested that the FDA not approve other ANDAs until the end of the 180-day exclusivity period.[51] In each of these cases, the FDA must (unless delay would be necessary to protect the public health) respond to 505(q) petitions within 150 days of filing.[52]

Section 505(q) also grants the FDA power to summarily dispose of a petition it finds was filed with the primary intent of delaying the approval of a generic and "on its face" does not raise a valid scientific or regulatory concern.[53] Despite denying nearly all petitions (as we show below[54]), the FDA has never invoked this power.

B. Congressional Reports

The FDAAA mandates that the FDA submit annual reports

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[48] Food and Drug Administration Safety and Innovation Act ("FDASIA"), Pub. L. No. 112-144, 126 Stat. 993 (2012).

[49] *See infra* Section III.C.

[50] *E.g.*, Citizen Petition, Docket No. FDA-2014-P-0099 (filed on January 10, 2014).

[51] *E.g.*, Citizen Petition, Docket No. FDA-2013-P-1623 (filed on December 9, 2013).

[52] 21 U.S.C. § 355(q)(1)(F).

[53] 21 U.S.C. § 355(q)(E)(1).

[54] *See infra* Section III.D.

to Congress summarizing trends and data on 505(q) petitions.[55] These reports must include the number of 505(q) petitions filed, the number of applications approved, the number of applications delayed due to citizen petitions, and the number of days each application was delayed.[56] As of the date of this article, seven reports have been submitted to Congress.

Employing a narrow definition of delay, the reports note that six petitions since fiscal year 2008 have caused the FDA to delay generic approval.[57] According to the reports, these six petitions delayed the approval of eight generic drug products. The amount of delay ranged from 9 days to 138 days.[58] The FDA has not indicated which generics were delayed.

In its most recent report to Congress, the FDA stated that it "continues to be concerned that section 505(q) is not discouraging

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[55] *Id.*

[56] *Id.*

[57] *Report to Congress: Eighth Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2015*, July 29, 2016 [hereinafter FY 2015 Report]; *Report to Congress: Seventh Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action*, Aug. 3, 2015 [hereinafter FY 2014 Report]; *Report to Congress: Sixth Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2013* [hereinafter FY 2013 Report]; *Report to Congress: Fifth Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2012* [hereinafter FY 2012 Report]; *Report to Congress: Fourth Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2011* [hereinafter FY 2011 Report]; *Report to Congress: Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action For Fiscal Year 2010* [hereinafter FY 2010 Report]; *Report to Congress: Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action For Fiscal Year 2009* [hereinafter FY 2009 Report]; *Report to Congress: Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action For Fiscal Year 2008* [hereinafter FY 2008 Report].

[58] FY 2013 Report, *supra* note 57, at 3; FY 2011 Report, *supra* note 57, at 3; FY 2010 Report, *supra* note 57, at 3; FY 2009 Report, *supra* note 57, at 4; FY 2008 Report, *supra* note 52, at 4.

the submission of petitions that are intended primarily to delay the approval of competing drug products and do not raise valid scientific issues."[59] Evidence that citizen petitions are used to delay generic entry can be inferred from the vast number of petitions that the FDA denies.

C. Initial Study

In our earlier study, the first empirical study of citizen petitions, we reviewed every petition filed with the FDA between 2001 and 2010. We found that petitions increased through the decade, with a total of 258 petitions filed.[60] We observed that 68% of petitions were filed by brand companies, and that more than 3/4 of brand petitions targeted generic drugs.[61]

We concluded that the FDA granted 19% of citizen petitions and denied 81%.[62] Generic petitions were more successful, with 28% granted and 72% denied, than brand petitions, with 19% granted and 81% denied.[63]

Our earlier study found that the FDAAA had not been successful in reducing the number of petitions. After the legislation was enacted, the average number of filings per year increased from 27 to 34.[64] Brand petitions against generics increased from 9 to 16 per year.[65] And the grant rate for brands' petitions against generics declined from 20% to 19%.[66]

This Article picks up where the original study left off. One change in the citizen-petition universe is the 2007 enactment of section 505(q). Because brand firms sometimes targeted other brands rather than generics, our earlier study analyzed the targets of

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[59] FY 2015 Report, *supra* note 57, at 8.

[60] Carrier & Wander, *supra* note 1, at 270.

[61] *Id.* at 270-71.

[62] *Id.* at 274.

[63] *Id.* at 275-76.

[64] Carrier & Wander, *supra* note 1, at 282.

[65] *Id.*

[66] *Id.*

citizen petitions. In contrast, 505(q) petitions, by definition, target generics.

III. GRANTS/DENIALS 2011-15

This Part offers empirical research on the FDA's grants and denials of citizen petitions between 2011 and 2015. It begins by offering a brief summary of the methodology we used, both in general and in relation to mixed decisions. It then explores the total number of 505(q) petitions. And it concludes by surveying petitions' success rate in general and among brand firms in particular.

A. Methodology: General

We tracked citizen petitions by using the industry-standard compilation available at FDA Law Blog.[67] This website maintains an ongoing record of petitions filed with the FDA. Known as the FDA Citizen Petition Tracker,[68] the dataset is regularly updated with newly filed petitions as well as the FDA's disposition of the petitions.

Given that our previous study concluded in 2010, we begin with petitions filed in 2011.[69] And we end with 2015, the last full year for which information is available.

Within this timeframe, we focus on petitions in the "Drug" category.[70] And within this category, we limit our analysis to 505(q)

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[67] FDA Law Blog, http://www.fdalawblog.net/ (last visited Aug. 5, 2016).

[68] The Tracker includes the following data: Docket Number, Petitioner, Product Name/Issue, Category, Petition Type, Receipt Date, Decision Date, and Decision. We last reviewed the FDA Citizen Petition Tracker on August 2, 2016. As of that date, the Tracker's dataset had been updated on May 26, 2016; November 13, 2015; May 10, 2016; April 20, 2016; and July 25, 2016, for the years 2011 through 2015 respectively.

[69] *See* Carrier & Wander, *supra* note 1.

[70] Starting in 2013, the Citizen Petition Tracker began to track all petitions filed with the FDA and categorized them under the categories of "Drug," "Animal Drug," "Food," "Biologics," "Dietary Supplement," "Medical Device," "Tobacco," and "Misc."

petitions.[71] As we mention above,[72] 505(q) petitions were created to

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[71] From the Tracker's 505(q) dataset, we excluded two types of petitions. First, we excluded petitions for which the Tracker noted that the FDA "does not consider this a 505(q) petition." *E.g.*, Citizen Petition, Docket No. FDA-2012-P-0895 (filed on Aug. 13, 2012). Second, we excluded the two petitions that were withdrawn within 7 days and refiled. Citizen Petition, Docket No. FDA-2012-P-0545 (filed on May 31, 2012) (petition aimed at LYRICA® generic withdrawn seven days later and refiled on June 6, 2012); Citizen Petition, Docket No. FDA-2011-P-0072 (filed on Feb. 8, 2011) (petition aimed at VENOFER® generic withdrawn two days later and refiled on Feb. 10, 2011).

In contrast, we included the six petitions for which withdrawal occurred more than seven days after the filing. For example, on July 16, 2012, Purdue Pharmaceuticals filed a petition aimed at a generic version of OxyContin. Citizen Petition, Docket No. FDA-2012-P-0760 (filed on July 16, 2012). This petition was withdrawn 79 days later on October 3, 2012 because Purdue had filed another petition in late August on the same subject matter. Citizen Petition, Docket No. FDA-2012-P-0939 (filed on August 29, 2012). This petition is worthy of attention since the total time of resolution, from the filing of the first petition to the FDA's denial of the second petition, spanned *191 days*—more than the statutory 150 days. We consider the July petition because the withdrawal and refiling of the petitions appears to have been strategic, as evidenced by the additional 41 days of FDA consideration. In other words, Purdue's petitioning strategy appears to have given the company two bites at the apple.

Nor is that all. Purdue filed a petition for reconsideration in 2013. Citizen Petition, Docket No. FDA-2012-P-0939 (filed on Feb. 22, 2013). This further reveals the firm's attempt to "double down" and extend the time FDA spent reviewing the challenged generic.

We found that the other five petitions for which withdrawal occurred more than seven days after filing raised similar concerns and included them in our dataset. Citizen Petition, Docket No. FDA-2012-P-0295 (filed on Mar. 26, 2012) (petition aimed at ELMIRON® withdrawn after 184 days); Citizen Petition, Docket No. FDA-2013-P-1399 (filed on Oct. 31, 2013) (petition aimed at SAPHRIS® withdrawn after 27 days and immediately refiled); Citizen Petition, Docket No. FDA-2013-P-1128 (filed on Sept. 12, 2013) (petition aimed at COPAXONE® withdrawn after 113 days); Citizen Petition, Docket No. FDA-2013-P-1082 (filed on Sept. 4, 2013) (petition aimed at RAYOS® withdrawn after 30 days); Citizen Petition, Docket No. FDA-2014-P-1302 (filed on July 11, 2014) (petition aimed at DICLEGLIS® withdrawn after 70 days).

[72] *See supra* notes 45-54**Error! Bookmark not defined.** and accompanying text.

ensure that citizen petitions would not be abused to delay generic entry. Other types of petitions, such as ANDA Suitability and RLD Designation petitions, do not immediately pose such a threat and therefore fall outside the scope of this study.

B. Methodology: Mixed Decisions

One of the difficulties involved in reviewing FDA rulings on citizen petitions is that a number of petitions are not clear grants or denials. The FDA sometimes issues "mixed" decisions, which grant in part and deny in part the petition. Although these determinations technically are mixed, one of the findings is often a formality that has no practical significance. Building on the project we began in our previous article to analyze mixed decisions, we examine the 2011-2015 petitions to determine which mixed decisions were essentially granted and which were essentially denied.

We find that between 2011 and 2015, the FDA issued 23 mixed petitions. Based on a thorough review, we conclude that, of this group, the FDA essentially granted 6 petitions and essentially denied 17. In the data we offer below, we treat essentially granted/denied petitions as if they were formally granted or denied.

The types of mixed decisions we reviewed in this survey are similar to those noted in our previous article. For example, the FDA often"grants" requests for additional information regarding industry guidance while denying the more substantive aspect of the petition. One example is provided by Physical Pharmaceuticals' and Allergan's separate petitions regarding the multi-billion dollar immunosuppressant, RESTASIS®.[73] The companies asked the FDA to reevaluate its draft bioequivalence recommendations and deny ANDAs referencing the brand drug RESTASIS® that lacked certain additional studies or analysis.

In a forty-five page response, the FDA denied petitioners' requests for the FDA to revise its guidelines for ANDA approval to require additional testing to prove bioequivalence. The agency also denied petitioners' request to reject any ANDAs that lacked this

[73] Citizen Petition, Docket No. FDA-2015-P-1404 (filed on Apr. 24, 2015); Citizen Petition, Docket No. FDA-2014-P-0304 (filed on Feb. 28, 2014).

testing. And it "determined it has clear legal authority to review and approve an ANDA for cyclosporine ophthalmic emulsion" that relies on the testing in its bioequivalence guidelines.[74]

Despite all of these clear indications that it was denying the petition, the FDA also "granted" an aspect of the petition that technically put it in the "mixed" category. The agency granted petitioners' non-substantive request to "disclose the in vitro bioequivalence methods the Agency intends to apply or accept for ANDAs that refer to RESTASIS®" and not approve any ANDA referencing RESTASIS® unless the FDA first responds to findings from Allergan's experimental test emulsions.[75] This petition only seeks information from the agency rather than targeting the generic drug itself. Because the FDA's decision did not grant any of the requests for additional testing by the ANDA applicant, and only granted the request for more information from the FDA itself, we treat the petition as "essentially denied."

Another example is provided by a petition filed by Abbott Laboratories against testosterone gel AndroGel®.[76] Abbott asked the FDA to revisit its therapeutic equivalence ("TE") ratings, which are ratings the agency uses to state that a drug is therapeutically equivalent to another drug. Abbott also requested that the FDA require additional bioequivalence studies and refrain from granting TE ratings for drugs until it had revised these rules.

The FDA denied Abbott's request on the grounds that additional notice-and-comment rulemaking to revisit its long-established approach to TE ratings is "not necessary or appropriate."[77] The agency also denied Abbott's lengthy requests for reevaluation of other companies' topical testosterone gel

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[74] FDA Response to Physical Pharmaceuticals and Allergan's Citizen Petitions, Docket No. FDA 2015-P-1404, at 44 (Feb. 10, 2016), *available at* https://www.regulations.gov/document?D=FDA-2015-P-1404-0007.

[75] *Id.*

[76] Citizen Petition, Docket No. FDA-2011-P-0610 (filed on Aug. 19, 2011).

[77] FDA Response to Abbott Laboratories Citizen Petition, Docket No. FDA-2011-P-0610, at 18 (June 23, 2015), *available at* https://www.regulations.gov/document?D=FDA-2011-P-0610-0010.

interchangeability status or labels.[78]

But the FDA "granted" one aspect of Abbott's petition. Because possible variations of approved labeling for topical gel testosterone products could "cause confusion," the FDA "intend[ed] to consider further these labeling differences in [its] on-going efforts to harmonize the approved labeling for drug products in the same class."[79] In other words, the FDA denied all the petitioner's substantive requests that would affect competing products while merely agreeing to keep certain labeling considerations in mind.

In other instances, the FDA "essentially grants" petitions that raise safety issues. For example, on May 31, 2011, Lehigh Valley Technologies ("Lehigh") and Glenmark Generics, Inc. ("Glenmark") jointly filed a petition regarding oxycodone HCL pain relievers (such as Oxycontin®, Roxicodone® and Oxecta®).[80] The petitioners requested that the FDA refrain from approving any ANDA or NDA for a single entity oxycodone hydrochloride unless the active pharmaceutical ingredient ("API") satisfied certain impurity limits.[81] The petition also requested that the API meet these specific impurity limits under "accelerated stability conditions for 6 months" and, in the event any ANDA or NDA did not meet such impurity limits, that the FDA stay any approval until data was submitted establishing the product's safety.[82]

The FDA agreed with Lehigh and Glenmark that certain impurities in opioid substances had been a concern, and that this was the third petition to address these impurities. The agency had "been working to lower the levels of these potentially genotoxic impurities since 2002" and, accordingly, granted the petitioners' request to require any oxycodone HCL products to establish specific

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[78] *Id.* at 23-24, 28-29, 33.

[79] *Id.* at 33.

[80] FDA Response to Lehigh and Glenmark Citizen Petition, Docket No. FDA-2011-P-0433, at 1-2 (Nov. 21, 2011), *available at* https://www.regulations.gov/document?D=FDA-2011-P-0433-0005.

[81] *Id.* Specifically, Lehigh and Glenmark requested that the API satisfy specific impurity limits for α,β-unsaturated ketones (otherwise referred to as "ABUKs"), which the FDA refers to as "genotoxic impurities." *Id.*

[82] *Id.* at 1.

impurity limits or submit toxicology studies confirming that any impurities would not be expected to be carcinogenic or mutagenic.[83]

The FDA, however, denied petitioners' request that the applicants' impurity profiles match those of the referenced product, explaining that it does not "require that ANDA or 505(b)(2) applicants use the same chemical synthesis or manufacturing process" as the referenced product and that not all products should be held to "identical standards."[84] The FDA also denied petitioners' request for additional stability testing, finding that this was not likely to provide useful data and stating that, based on the available information, the impurities at issue were not expected to increase over time.[85]

We characterized this petition as "essentially granted" because the FDA agreed with the petitioners that the ANDA applicant establish certain impurity limits before approval. The agency agreed with the petitioners that "[i]t is in the interest of public health and consistent with Agency policy that applicants for single ingredient oxycodone HCL product meet this standard."[86]

C. Total 505(q) Petitions

With the methodology behind us, we begin with the total number of 505(q) citizen petitions filed each year from 2011 through 2015. Table 3 presents every petition labeled "Citizen Petition (505(q) Certification)" that appeared in the FDA Citizen Petition Tracker.[87] In the five-year period, between 17 and 37 petitions were filed each year. The mean and median number of filings was 25. The filings peaked in 2013, with 37, and fell to 17 in 2015.

Table 3 further breaks down the identity of the party that files 505(q) petitions. Of the 124 petitions, there were 118 different

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[83] *Id.* at 2.

[84] *Id.* at 2, 9.

[85] *Id.* at 2, 10-11.

[86] *Id.* at 2.

[87] http://www.fdalawblog.net/ (last visited Aug. 5, 2016).

filers.[88] Table 3 shows that brand companies file the vast majority, 92%, of 505(q) petitions.

The other 8% were filed by generics challenging the entry of competing generics or interest groups challenging drug safety. For example, a generic could file a petition relating to ANDA suitability, such as when it requests the FDA to allow the generic to differ from the reference drug. These types of petitions do not present similar anticompetitive concern and lie outside the scope of this study.

The fact that brand firms file more than 9 out of 10 505(q) petitions is concerning. If 505(q) petitions were serving their intended purpose of ensuring the safety and efficacy of generic drugs, we should observe interest groups and competing generic firms filing a significant share of the petitions. That is not the case.[89]

[88] The 124 petitions were filed between 2011 and 2015. The lower figure of 79 petitions in Table 2 reflects those filed between 2013 and 2015. *See supra* note 40.

[89] It is conceivable that interest groups and competing generics could file fewer 505(q) petitions as a result of filing petitions at other times. By filing petitions challenging safety or efficacy at times when there is not a pending ANDA, such petitions could potentially displace 505(q) petitions.

Table 3
505(q) Petitions and Petitioners[90]

	Total Number of Petitions	Number of Petitioners	Brand Petitions	Generic/Other Petitions
2011	18	18	17	1
2012	27	26	24	2
2013	37	32	30	2
2014	25	25	21	4
2015	17	17	16	1
Total	124	118	108	10
Percentage		100%	92%	8%

D. Success Rate

Our previous study found that the FDA denied 81% of petitions, granting only 19%.[91] Remarkably, *the denial rate has plummeted, even from that low rate*. Between 2011 and 2015, the FDA

[90] In 2012 and 2013, there were more petitions than petitioners because a petitioner filed multiple petitions. For example, in 2012, Purdue Pharma filed two petitions targeting a generic version of OxyContin. *See supra note* 68; Citizen Petition, Docket No. FDA-2012-P-0939 (filed on Aug. 29, 2012). As a result, in 2012, there were 26 petitioners and 27 petitions. Likewise, in 2013, three petitioners filed two petitions each and one filed three petitions. *E.g.*, Citizen Petition, Docket No. FDA-2013-P-0247 (filed on March 4, 2013 and Aug. 23, 2013). As a result, in 2013, there were 32 petitioners and 37 petitions.

[91] *See* Carrier & Wander, *supra* note 1, at 274 tbl. 3.

issued 109 substantive decisions.[92] Strikingly, the FDA granted *only 8%* of 505(q) petitions, denying a full 92%.

Table 5 shows that the FDA denied 72% to 100% of petitions each year. In fact, the denial rate increased markedly after 2011, ranging between 94% and 100% a year from 2012 to 2015. In these four years, there were only, respectively, 1, 2, 1, and 0 petitions granted.[93]

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[92] While 124 505(q) petitions were filed between 2011 and 2015, the FDA has issued only 109 substantive decisions to date. *See infra* note 93.

[93] The categories "granted" and "denied" include mixed decisions that we determined to be essentially granted/denied. Table 4 does not include petitions that were withdrawn or are pending, or where the FDA issued an interim response with no substantive decision. There were 16 such petitions. As for withdrawn petitions, we recorded 0, 2, 3, 1, and 0 in the years 2011 through 2015 respectively. As for interim decisions, we recorded 0, 1, 2, 3, and 4 petitions from 2011 through 2015 respectively.

The grant and denial data differ slightly from what the FDA reported to Congress. One reason for the discrepancy is that the FDA's reporting period runs from October through September, while our data consists of petitions filed in a calendar year. In addition, we more closely parse mixed decisions. While the FDA reports merely state that a petition was resolved in part, our study looks more closely at the actual resolution. Since 2008, the FDA has reported that 66% of 505(q) petitions were denied, 5% granted, and 26% granted/denied in part. It is this 26% percent that we closely analyze and include in our grant/denial data. To reconcile the figures, going forward we suggest that the FDA release a list of citizen petitions along with its annual FDA report to Congress.

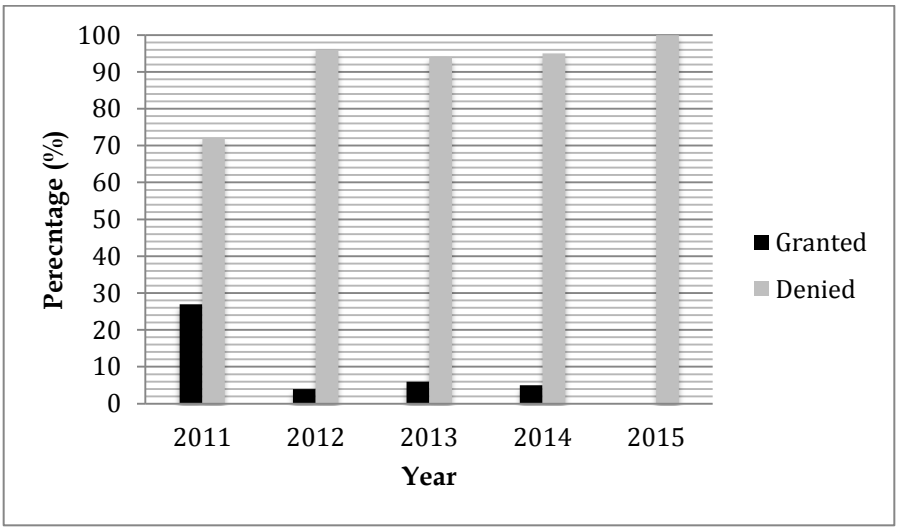
Table 4
Success Rate of Citizen Petitions[94]

	Granted		Denied	
2011	5	27%	13	72%
2012	1	4%	23	96%
2013	2	6%	31	94%
2014	1	5%	20	95%
2015	0	0%	13	100%
Total	9	8%	100	92%

Figure 1 presents these results graphically, providing another depiction of the lopsided results of the FDA's review of citizen petitions today.

[94] The number of denials and grants may differ from the number of petitions filed because the FDA may issue multiple decisions on a petition. *E.g.*, Citizen Petition, Docket No. FDA-2013-P-0371 (filed on Mar. 26, 2013) (for petition targeting testosterone gel Testim®, the FDA issued two mixed, "essentially denied," responses on July 23, 2014 and February 9, 2015).

Figure 1
Success Rate of Citizen Petitions



E. Brand Win Rate

The success rate in the previous section applies to all 505(q) petitions. Given that brand firms present the most direct concern of delaying generic entry, we examine the success rate for this category of petitions.

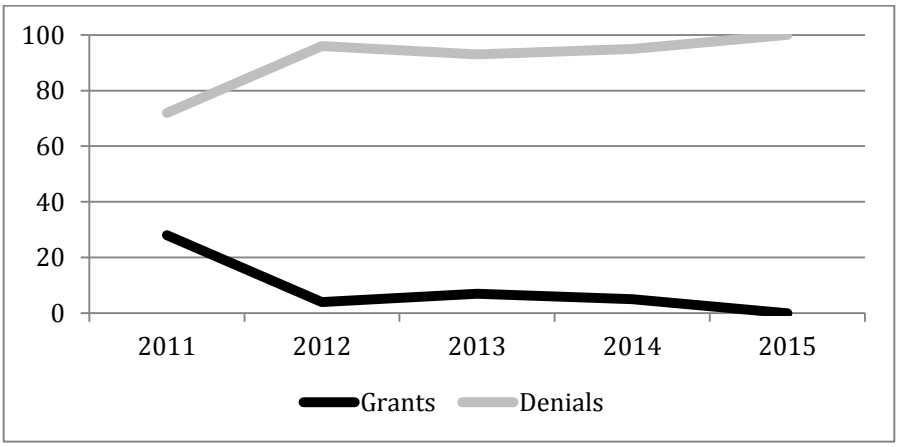
Figure 2 shows that between 2011 and 2015, the FDA considered 108 brand petitions. Of this universe (and not counting the 5 petitions that were withdrawn or are pending, or for which the FDA issued an interim response with no substantive decision), the agency granted 9 petitions (9%) and denied 94 (91%).

Because the number of 505(q) petitions not filed by brands is minimal, the results in this section are similar to those for all 505(q) petitions. The previous study showed that from 2001 through 2010, the FDA granted 22 brand petitions (19%) while denying 96 (81%).[95] Tracking the increased number of total 505(q) denials in the past five years, the brand success rate is roughly half what it was in the

[95] *See* Carrier & Wander, *supra* note 1, at 275.

previous decade.[96]

Figure 2
Brand Win Rate



IV. REASONS FOR INCREASINGLY QUESTIONABLE PETITIONS

Why have the grant rates fallen by more than half from the already-low 19% rate between 2001 and 2010? This Part explores three potential reasons. First, petitions are getting more complex. Second, many petitions are filed at the last-minute, shortly before the expiration of a patent or FDA exclusivity period. Third, the FDA resolves some petitions on the same day it approves the targeted generic.

A. Methodology

The new data we unearth in this Part calls for additional discussion of methodology. Once we narrowed down the universe to 505(q) petitions, we reviewed each petition and compiled four types of information.

First, we gathered data on the petition itself. This included information about the petitioner, the branded product that was the

[96] From 2011 through 2015, the FDA granted brand petitions 5, 1, 2, 1, and 0 times, in each year, respectively, for a total of 9. The agency denied petitions 13, 23, 28, 18, and 12 times, in each year, respectively, for a total of 94.

subject of the petition, and the type and length of the petition.

Second, we focused on the brand product that was the subject of the petition. In each citizen petition, a petitioner explains to the FDA the actions it is requesting. In the case of brand petitions, the company typically notes that it is the holder of a particular New Drug Application ("NDA") and asks the FDA to take a particular action on a pending generic application.

Once we determined the NDAs that were implicated by the petitions, we compiled the following expiration dates: (1) the listed patent closest to the petition's filing date, (2) the last-to-expire listed patent, *i.e.*, the "patent cliff" date, (3) the nearest data-exclusivity date[97] to the petition's filing, and (4) the last-to-expire listed data exclusivity.

We refer to these four dates as "exclusionary dates." We obtained these dates from the version of the Orange Book published *at the time of the petition's filing*. While some recent versions of the Orange Book are available online through an Internet search or by using Internet archives, the FDA's website provides only the most recent Orange Book information. As a result, it can be difficult to obtain data to assess those patents and data exclusivities protecting an approved drug at the time of a petition's filing. Because of these difficulties, we filed a Freedom of Information Act Request with the FDA and obtained pdf versions of all relevant Orange Books.

We used these versions to recreate the exclusionary-date environment at the time each petition was filed. For example, if a petition was filed on June 1, 2014, we obtained patent and exclusivity expiration dates from the Orange Books published in 2013 and 2014. Relying on the current version of the Orange Book would have yielded incomplete results because the FDA deletes patent and exclusivity dates that have expired.

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[97] The data-exclusivity date reflects periods of FDA exclusivity. A company that offers a drug with a new active ingredient is entitled to either four or five years of exclusivity, 21 U.S.C. §355(j)(5)(F)(ii), and new clinical investigations essential to approval (which include new dosage forms, new uses, and adoption of over-the-counter status) receive three years of exclusivity, 21 U.S.C. §355(c)(3)(E)(iii).

Third, we obtained information on any approved ANDA referencing the brand product at issue. Because a goal of our study is to assess the impact of citizen petitions on generic entry, we utilized the most up-to-date Orange Book information available on the FDA's website to determine ANDA data. Specifically, we kept track of ANDA approval dates to determine how often the FDA resolves a petition on the same day it approves the targeted ANDA. As we explain below,[98] this is important because same-day resolution raises the prospect of delayed ANDA approvals.

Fourth, and finally, we calculated the time difference between the petition's filing date and each of the four exclusionary dates. For example, if a petition was filed on June 1, 2014 and the only patent listed in the 2014 Orange Book for the brand product expired on June 8, 2014, the calculated time difference would be 7 days.[99]

Having narrowed the universe of petitions and obtained crucial data points, we determined that a significant number of petitions were "late-filed" petitions. We define such petitions as those filed within 6 months of an exclusionary date. While no single number axiomatically provides a boundary for the determination of late-filed petitions, a 6-month period makes sense because it targets "last-minute" petitions and is important in the pharmaceutical industry.

A 6-month period mirrors the timeframe of 180 days within which (before being reduced to 150 days) the FDA was required to

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[98] *See infra* Section IV.D.

[99] For an example, consider pain medication OFIRMEV. Cadence Pharmaceuticals filed a petition on November 4, 2013 regarding a prospective ANDA. In this case, we looked to the patent and exclusivities listed in the 33rd Edition of the Orange Book published in 2013 because this would have been the information available to the industry at the time of the petition's filing. Listed under OFIRMEV were two patents: U.S. Patent Nos. 6,028,222 and 6,992,218 expiring on August 5, 2017 and June 6, 2021, respectively. Also listed under the code "NP" ("new product") was an exclusivity of November 2, 2013. So at the time Cadence filed the petition on November 4, 2013, the '222 patent was set to expire in 1,370 days and the '218 patent was set to expire in 2,771 days. While these dates were far removed, the sole listed exclusivity had expired only 2 days before the petition's filing.

respond to 505(q) petitions. And it appears in the Hatch-Waxman Act's 180 days of exclusivity reserved for the first generic that files a "Paragraph IV" certification that the brand firm's patent is invalid or not infringed.[100] Finally, given that generic drugs typically take more than two years to develop and obtain FDA approval,[101] it is reasonable to assume that a petition filed within six months of an exclusionary date has the potential to affect a generic's development and approval strategy.

It bears mention that it is difficult for the FDA to provide a rapid analysis of science and law in its review of citizen petitions. This difficulty can cause the FDA to delay generic approval. Given that brand companies can make monopoly profits each day generic entry is delayed, it is often enough for a brand firm to merely delay generic entry rather than prohibit it. Filing within six months of generic approval increases the odds that the filing will delay generics.

It goes without saying that patent protection and data exclusivity underpin a drug product's lifecycle. We thus assume that the expiration of each of these periods could have a significant effect on competition in the market. In particular, the expiration of a patent or the data exclusivity period would be expected to lead to generic entry. And this naturally would result in the erosion of market share and a reduction in price, the magnitude of which would depend on the number of generics entering the market.[102] The filing of a petition close to the expiration period offers an indication that such expiration was a noteworthy event.

Because a brand firm will often list multiple patents in the Orange Book, a petition might be filed close to the expiration of one while another (or several) will not expire for years. We did not wish to introduce additional layers of complexity by examining each of the patents to reach an independent conclusion on their relative importance. Such a task would have required reading the patents, comparing them to those of rivals, and determining the likelihood of infringement. Further complicating such an analysis is the reality

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[100] 21 U.S.C. §355(j)(5)(B)(iv).

[101] *See* Carrier, *supra* note 27, at 1018.

[102] *See supra* notes 13-15 and accompanying text.

that not all patents listed in the Orange Book are litigated.

As an example of these potential difficulties, a brand firm could list multiple patents covering an active ingredient, a method of treatment, or a particular formulation. While a generic must show bioequivalence to the brand product to obtain approval, it does not necessarily follow that each patent listed in the Orange Book will be infringed. It thus is a fact-intensive exercise calling for significant discretion to determine whether a particular listed patent will be subject to litigation. In addition, some patents may only be implicated if the generic seeks approval for a particular indication. Similar issues arise with data exclusivity. All these considerations are case-specific and make it difficult to pinpoint a "most relevant" exclusionary date against which to compare a petition filing date.

As a result, our study takes a simple approach to the issue. If a petition is filed within six months of the expiration of an exclusionary date, we treat that date as being noteworthy. Rather than considering all the potential exclusionary dates, we use the actions of the brand—which will be aware of the approaching expirations—to determine the relevant dates.

B. Petition Complexity

Because they allege that a pending generic does not meet pharmacokinetic and bioequivalence standards, citizen petitions are inherently complex and challenging. The FDA, for obvious reasons, takes seriously petitions that claim that a potential generic drug poses safety concerns. With this in mind, petitioners seeking to delay or block a generic application (and keep their market share as a result) have an incentive to increase the complexity of their petitions to prolong FDA scrutiny.[103] For a blockbuster billion-dollar drug, delayed entry means millions of dollars extra *each day*.

We hypothesized that complex petitions could be used as a tool to complicate and delay generic entry. In the fact-specific setting of citizen petitions, complexity is difficult to quantify. As a proxy for complexity, we considered the one metric we could evaluate: petition length. All else equal, longer petitions would tend to slow

[103] In certain cases, in fact, the FDA asserts that additional time is needed to evaluate the complex issues raised by a petition.

down the FDA, which is forced to spend more resources reviewing lengthy petitions. In fact, congressional reports have continually explained that complex citizen petitions are draining the agency of time and resources better allocated to other functions.[104]

Along those lines, it is concerning that, as seen in Table 6, the average length of a 505(q) petition has more than doubled from 2011 to 2015, from roughly 14 to 32 pages.[105] This trend is accelerating, increasing between 2011 and 2015 from 14 to 21, 21, 26, and 32 pages.

Table 6
Average Page Length

	Length
2011	14
2012	21
2013	21
2014	26
2015	32

While petitioners could theoretically claim that longer petitions reflect increased complexity and therefore more legitimate petitions that have a greater likelihood of success, the reality is exactly the opposite. In fact, petitions that are longer than average show a reduced likelihood of success, *even in a universe in which only 8% of petitions are granted*.

In a remarkable finding, as shown in Table 7, only 1 petition

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[104] *See* FY 2014 Report, *supra* note 57, at 7.

[105] We ignored differences between single-spaced and double-spaced petitions, and also did not include appendices.

with a page length above the mean was granted in five years. Not including the 9 petitions in the "other" category (which were subject to an interim response or withdrawn), the ratio of 1 grant to 30 denials, for an anemic grant rate of 3%, speaks volumes.

Table 7
Results for Long Petitions

	Granted	Denied	Other[106]
2011	1	5	0
2012	0	9	1
2013	0	8	3
2014	0	5	2
2015	0	3	3
Total	1	30	9

A review of the petitions that have been granted shows the higher success of shorter petitions. In 2011, when the average page length was 14, the 5 granted petitions were 12, 22, 6, 5, and 8 pages.[107] In 2012, when the average page length was 21, the only granted petition was 7 pages.[108] In 2013, when the average page length was 21, the two granted petitions were 13 and 6 pages.[109] And

[106] The "Other" category includes withdrawals and interim responses.

[107] Citizen Petition, Docket No. FDA-2011-P-0767 (filed on Oct. 20, 2011); Citizen Petition, Docket No. FDA-2011-P-0575 (filed on Aug. 1, 2011); Citizen Petition, Docket No. FDA-2011-P-0433 (filed on May 31, 2011); Citizen Petition, Docket No. FDA-2011-P-0127 (filed on Mar. 1, 2011); Citizen Petition, Docket No. FDA-2011-P-0120 (filed on Feb. 28, 2011).

[108] Citizen Petition, Docket No. FDA-2012-P-0647 (filed on June 19, 2012).

[109] Citizen Petition, Docket No. FDA-2013-P-0995 (filed on Aug. 12, 2013); Citizen Petition, Docket No. FDA-2013-P-0664 (filed on June 4, 2013).

in 2014, when the average page length was 26, the only granted petition was 15 pages.[110] In sum, long petitions seem geared not to raising legitimate safety concerns but to bogging down the FDA and delaying generic entry.

C. Petitions and Exclusionary Dates

In addition to long petitions, we examined the point in a brand drug's lifecycle when a 505(q) petition is filed. For the 124 petitions filed between 2011 and 2015, 129 separate NDAs were protected.[111] We analyzed the exclusionary dates when these 129 NDAs likely would lose market share as a result of the approval of a pending generic (which is the subject of a 505(q) petition)—*i.e.*, the *protected* NDA.

We focused on petitions filed within 6 months of an exclusionary date (either patent- or exclusivity-related) of the brand product. We found that from 2011 through 2015, there was a petition filed within this "late-filed" window for roughly two-fifths of the protected NDAs.

Our research reveals that of the 129 protected NDAs, a citizen petition was filed within 6 months of an exclusionary date in 50 cases, or 39%. 19% had a petition filed with 6 months of a patent expiration date. 24% witnessed a petition within 6 months of a data exclusivity date. And 4% had a petition filed within 6 months of both a patent expiration and data exclusivity date.[112] Table 8 presents our findings.

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[110] Citizen Petition, Docket No. FDA-2014-P-1269 (filed on Aug. 18, 2014). No petitions were granted in 2015.

[111] There are more NDAs implicated than number of petitions because a single petition can implicate more than one NDA. *E.g.*, Citizen Petition, Docket No. FDA-2013-P-0664 (filed June 4, 2013) (implicating NDA 20756 and 20757).

[112] The 39% figure is reached by combining the 19% and 24% figures and (to avoid double-counting) subtracting the 4%.

Table 8
Petitions and Exclusionary Dates[113]

	2011	2012	2013	2014	2015	Total
Number of Protected NDAs	22	30	32	25	20	129
Within 6 Months of Nearest Patent	2 (8%)	3 (10%)	7 (22%)	5 (20%)	4 (20%)	21 (16%)
Within 6 Months of Final Patent	0 (0%)	0 (0%)	1 (3%)	2 (8%)	1 (5%)	4 (3%)
Within 6 Months of Nearest Exclusivity	4 (18%)	2 (7%)	5 (16%)	3 (12%)	2 (10%)	16 (12%)
Within 6 Months of Final Exclusivity	3 (14%)	5 (17%)	6 (19%)	1 (4%)	1 (5%)	16 (12%)
Within 6 months of Patent and Exclusivity	2 (9%)	1 (3%)	2 (6%)	0 (0%)	0 (0%)	5 (4%)

[113] We avoid double-counting in the table in several ways. First, we do not double-count protected NDAs for which a petition was filed within six months of the final patent that also was the nearest patent. We include that scenario only in the "final patent" row. We apply the same treatment to instances in which the final exclusivity date is also the nearest exclusivity date. Finally, in settings in which petitions fall within 6 months of *both* patent and data exclusivity expiration, we include that only in the penultimate row of the table.

Date						
Within 6 months of an Exclusionary Date	6 (27%)	9 (30%)	17 (53%)	10 (40%)	8 (32%)	50[114] (39%)

As for patent-specific exclusionary dates, 16% of NDAs witnessed a petition filed with 6 months of the nearest patent expiration, while 3% had a petition filed within 6 months of the patent cliff. The prevalence of patents filed within 6 months of the nearest patent, rather than the patent cliff, makes sense.

The Hatch-Waxman Act is predicated on a generic's willingness to file an ANDA as soon as data exclusivity expires. By offering 180 days of exclusivity, the generic is incentivized to challenge the validity of any patents listed in the Orange Book. Brand companies often list numerous patents with varying expiration dates.

Research and development takes time and a brand firm's most important discovery—for which it invariably obtains patent protection—is the active ingredient compound. Because patents can be granted long before the FDA approval process begins, those claiming the active ingredient are promptly listed in the Orange Book after the drug's approval. But because the term of that patent began to run years earlier, it could expire around the time data exclusivity runs out. These active-ingredient patents expire first because the drug product tends to be discovered (and the patent

[114] The total of 50 petitions within 6 months of an exclusionary date is reached by (1) adding the 25 petitions filed within 6 months of a patent to (2) the 32 petitions filed within 6 months of an exclusivity date and (3) subtracting the 5 petitions filed within 6 months of a patent *and* exclusivity date and (4) subtracting the 2 petitions that were each filed within 6 months of two *separate* exclusionary dates, Citizen Petition, Docket No. FDA-2011-P-0840 (filed on Nov. 18, 2011) (petition on PREVACID 24 HR, NDA 020406, filed within 21 days of nearest exclusivity date and 162 days of final exclusivity date); Citizen Petition, Docket No. FDA-2014-P-1649 (filed on Sept. 30, 2014) (petition on FUSILEV, NDA 020140, filed within 154 days of nearest exclusivity date and 178 days of final exclusivity date).

term begins to run) years before the review and approval phase.

In contrast, last-to-expire patents—in other words, those making up the "patent cliff"—typically do not cover a product's main active ingredient but instead claim secondary subject matter that may be related to the process of how the drug is made or can be formulated.[115] Because a brand can list a patent in the Orange Book at any point, it will continue prosecuting these secondary patents throughout the drug's lifecycle and list those patents many years after data exclusivity or main active ingredient patents expire.[116]

These observations on the nature of drug patents are consistent with our findings. The ANDA approval process necessarily occurs after the relevant exclusivity expires, with the main active ingredient patents often having expired as well. As a result, a petition challenging that approval process is more likely to occur closer to the expiration of nearest patents.[117] This aligns with our findings of more petitions being filed within six months of the nearest, rather than final, patent.

With regards to exclusionary dates related to data

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[115] For example, in the case of ABILIFY®, Otsuka Pharmaceuticals filed a petition within 40 days of the expiration of U.S. Patent No. 5,006,528, which claims a compound. Citizen Petition, Docket No. FDA-2014-P-1354 (filed on Sept. 10, 2014). The last-to-expire patent listed in the 2014 Orange Book, however, was slated to expire more than 3,000 days later, on December 16, 2024. This patent, U.S. Patent No. 8,017,615, claims a process for developing a pharmaceutical preparation. To state the obvious, the '615 patent is not as strong as a patent claiming a compound. *See* MARTIN VOET, THE GENERIC CHALLENGE: UNDERSTANDING PATENTS, FDA AND PHARMACEUTICAL LIFE-CYCLE MANAGEMENT 70 (4th ed. 2014) (explaining that "[t]he best pharmaceutical patent is a compound patent" because "it covers a drug product no matter how it is formulated, no matter how it is made, no matter what it is sold for, and no matter what use it is put to").

[116] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-0181 (filed on Jan. 16, 2015) (petition aimed at Mylan's EpiPen® with Orange-Book listed-patents first listed only in 2009—more than *two decades* after EpiPen® was first approved in 1987).

[117] As discussed below, see *infra* Section V.B, petitions are also filed soon before patent cliffs.

exclusivity, we determined that 12% of protected NDAs had a petition filed within 6 months of their nearest exclusivity date, and 12% of NDAs had a petition filed within 6 months of the latest exclusivity to expire.

Eliminating duplication in cases in which there was both patent and data exclusivity, we conclude that 39% of all protected brand products—*i.e.*, those products likely to lose market share as a result of the generic application at issue—had a 505(q) petition filed within 6 months of an exclusionary date. Such a finding raises a question as to whether the petitions were related to safety concerns or whether they were just another tool in the toolkit of "lifecycle management" (less charitably known as potentially anticompetitive behavior).

Strikingly, as seen in Table 9, the FDA denied *49 of 50* petitions filed within 6 months of a protected NDA's exclusionary date.[118] This paltry 2% grant rate further supports our hypothesis that late-filed petitions almost never raise valid safety concerns.

Table 9
Grant/Denial of Petitions Filed
Within 6 Months of Exclusionary Date

	2011	2012	2013	2014	2015	Total
Grant	0	0	1	0	0	1
Denial	6	9	16	10	8	49

D. Same-Day Resolution of Petition and ANDA Approval

Another recent occurrence is the FDA's resolution of the citizen petition on the same day (or in the same month) it approves

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[118] For the sole grant, see Citizen Petition, Docket No. FDA-2013-P-0995 (filed on Aug. 12, 2013) (mixed, "essentially granted," decision, in which FDA determined that application seeking approval for generic Suboxone should include data proving minimal impurities).

an ANDA. The concern in this scenario is that generic entry could be delayed because the FDA does not approve the ANDA until it resolves the citizen petition.[119]

As we show in Table 10, the FDA approved 23 targeted ANDAs within one month after it resolved the petition raising concerns about the ANDA. Of these 23 ANDAs, 6 were approved on the *same day* the FDA resolved the petition targeting the generic. The 11 petitions affected an additional 17 ANDAs, which were approved within one month of the ruling on the petition. *In every case where same-day (or even same-month) resolution and generic approval occurred, the 505(q) petition was denied.*

This trend has increased recently, with the FDA approving 3 ANDAs on the same day it resolved a petition in 2015. This reflects as many same-day resolutions as the previous 4 years combined.

[119] The Second Circuit rejected a claim that a brand's citizen petition amounted to sham litigation on the grounds that the FDA resolved a citizen petition on the same day the ANDA was approved. Apotex Inc. v. Acorda Therapeutics, Inc., 823 F.3d 51, 59 (2d Cir. 2016) (reasoning that agency's guidance on 505(q) petitions "tends to undermine the inference . . . that when a citizen petition is denied simultaneously with the grant of an ANDA petition, the citizen petition was a sham and an anticompetitive weapon"). But even if the confluence of FDA resolution of a petition and ANDA approval does not *automatically* demonstrate that litigation is a sham (based on a test with rigorous objective and subjective components), it still could *support* a finding of delayed generic entry.

Table 10
Same-Month Resolution of Petitions and ANDA Approval

	Number of Petitions	ANDA Approved on Same Day	Additional ANDAs Approved within One Month	Petitions Granted
2011	4	2	13[120]	0
2012	1	1	0	0
2013	1	0	1	0
2014	0	0	0	0
2015	5	3	3	0
Total	11	6	17	0

While it is difficult to precisely delineate causation, the mere fact that the FDA waits to approve an ANDA until it denies a citizen petition raises concerns. It makes sense that the FDA would not be willing to grant generic approval until it resolves safety issues. If the FDA has not resolved an issue related to the bioequivalence of a generic drug, it cannot approve the ANDA.

But the FDA may be hesitant to deny a citizen petition early on the grounds that this would give the brand firm the ability to challenge the petition denial in court. The denial of a citizen petition is a final agency action under the Administrative Procedures Act, which means an Article III court can review and reverse the agency's determination. Challenging the FDA's

[120] This number is high because on March 27, 2011, the FDA approved 10 separate generics referencing AstraZeneca Pharmaceuticals' SEROQUEL®. This appears to be an outlier.

actions in court provides the brand company with another avenue to delay entry of the generic drug through legal proceedings.

As a result, the FDA may have adopted a preferred strategy of (1) denying a citizen petition and (2) approving a generic drug on the same day. One interpretation of this simultaneous resolution is that the petition does not delay generic entry because approval comes no later than the resolution of the petition. As a result of simultaneous resolution, moreover, the brand may not have an incentive to appeal in court since the generic has already penetrated the market, with the "damage" having already occurred. Nonetheless, resolving the citizen petition on the same day (or within the same month) that it grants ANDA approval can still raise the suspicion that the FDA delayed approval until it dealt with the petition.

The cases involving simultaneous resolution in 2015 provide examples of potential delay. In that year, 3 of the 5 petitions the FDA resolved in the same month it approved the ANDA were filed within 6 months of an exclusionary date.[121] As for the other two petitions, one dealt with Teva's multi-billion-dollar drug COPAXONE®. As we discuss below,[122] Teva filed eight separate petitions asking the FDA to take actions on any ANDA referencing COPAXONE®. The fifth petition was resolved four days

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[121] Teva Pharmaceuticals filed a petition within 36 days of an exclusivity date protecting TREANDA®. Citizen Petition, Docket No. FDA-2015-P-3980 (filed on Mar. 24, 2015). The FDA ultimately denied this petition on March 24, 2016—the same day it approved two generics: ANDA 204771 and ANDA 205476. And Helsinn Healthcare filed two separate 505(q) petitions targeting a proposed generic for ALOXI® within 30 days of the nearest patent listed in the Orange Book. Citizen Petition, Docket No. FDA-2015-P-1722 (filed on May 13, 2015); Citizen Petition, Docket No. FDA-2015-P-1721 (filed on May 13, 2015). The FDA denied these petitions on October 9, 2015 and approved two generics four days later on October 13, 2015: ANDA 202521 and ANDA 090713.

[122] *See infra* Section V.A. On April 1, 2015, Teva filed the last of its 8 petitions targeting Sandoz's generic application referencing COPAXONE®. 15 days later, on April 16, 2015, the FDA denied the petition and simultaneously approved Sandoz's ANDA.

before ANDA approval.[123] Again, in *every case* in which the FDA resolved a petition within the same month it approved the generic, it denied the petition.

One explanation for the increase in same-day resolution of petition and ANDA approval may be the FDA's recent backlog in generic applications. Recently, approval timelines for ANDAs have slowed from 30 months to 48 months.[124] Time will tell whether 2015 marks a trend of increasing simultaneous resolution.

V. EXAMPLES

The concerns mentioned above are not hypothetical. This Part introduces four examples that illustrate the role citizen petitions play in brand firms' toolkits to delay and block generic competition towards the end of a product's lifecycle. It provides examples of (1) serial petitions; (2) egregious examples of citizen petition filings close to exclusionary dates; (3) the combination of citizen petitions and product-hopping; and (4) the combination of citizen petitions and drug patent settlements.

A. COPAXONE®: Serial Petitions

In patent law, certain case names—such as *Markman*, *Festo*, and *Panduit*—instantly become classic. In 2015, *Teva v. Sandoz* joined that list when the Supreme Court held that a district court's resolution of subsidiary factual matters made in the course of its construction of a patent claim are reviewed for clear error, and not *de novo*.[125] Underlying this important ruling is a story of Teva's robust life cycle management of COPAXONE®—the $3 billion/year multiple sclerosis drug.

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[123] Citizen Petition, Docket No. FDA-2015-P-1721 (filed on May 13, 2015).

[124] Zachary Brennan, *FDA's Woodcock: Generic Drug Application Backlog Will be Eliminated Before GDUFA II*, RAPS, Jan. 28, 2016, http://www.raps.org/Regulatory-Focus/News/2016/01/28/24195/FDA%E2%80%99s-Woodcock-Generic-Drug-Application-Backlog-Will-be-Eliminated-Before-GDUFA-II/#sthash.AdVBkhWG.dpuf.

[125] 135 S. Ct. 831 (2015).

First approved in December 1996, Teva faced intense market pressure to combat generic entry as its data exclusivity was due to expire in the mid-2000s and patent protection would lapse in 2014. Once generics filed for approval, Teva initiated patent litigation under the Hatch-Waxman Act. But in addition to litigation, the company—in an action that has not received much attention—also filed *eight* separate citizen petitions with the FDA from 2008 through 2015.

Teva's efforts to protect COPAXONE® present a particularly glaring example of a company's aggressive use of the citizen petition process. For starters, there were two petitions of more than 130 pages in length.[126] And in each of the eight petitions,[127] Teva argued that the FDA should refuse to approve a generic version of COPAXONE®—unless certain criteria were met—because the drug was highly complex and therefore no generic could produce the "same active ingredient."[128] One aspect that Teva continually stressed was the lack of bioequivalence testing available for non-biological complex drugs.[129] The FDA nonetheless denied each of the eight petitions. The final denial came on the same day the FDA approved Sandoz's ANDA.

Looking forward, this type of serial petitioning may herald the wave of the future in the emerging biosimilar industry. As of mid-2016, the majority of citizen petitions in the biosimilar industry have dealt with FDA labeling regulations.[130] Because biosimilars aim

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[126] Citizen Petition, Docket No. FDA-2015-P-1050 (filed on April 1, 2015) (133 pages); Citizen Petition, Docket No. FDA-2014-P-0933 (filed on July 2, 2014) (132 pages).

[127] Citizen Petition, Docket No. FDA-2015-P-1050 (filed on April 1, 2015); Citizen Petition, Docket No. FDA-2014-P-0933 (filed on July 2, 2014); Citizen Petition, Docket No. FDA-2013-P-1641 (filed on Dec. 5, 2013); Citizen Petition, Docket No. FDA-2013-P-1128 (filed on Sept. 12, 2013); Citizen Petition, Docket No. FDA-2012-P-0555 (filed on June 4, 2012); Citizen Petition, Docket No. FDA-2010-P-0642 (filed on Dec. 10, 2010); Citizen Petition, Docket No. FDA-2009-P-0555 (filed on Nov. 13, 2009); Citizen Petition, Docket No. FDA-2008-P-0529 (filed on Sept. 26, 2008).

[128] Citizen Petition, Docket No. FDA-2015-P-1050 (filed Apr. 1, 2015).

[129] *Id.*

[130] *E.g.*, Citizen Petition, Docket No. FDA-2015-P-5022 (filed Dec. 22, 2015).

to be similar and not identical to brand biologics, it is quite likely we will see more brand firms filing citizen petitions similar to those Teva filed in relation to COPAXONE®.[131]

B. MIRENA®: Filing Immediately Before Patent Expiration

One example of the last-minute filings we discussed above[132] appears in the case of MIRENA®, a long-acting intrauterine device (IUD). Originally approved on December 6, 2000, the product can cost nearly $1000 and is the only hormonal release IUD in the U.S. market that provides birth control for more than six years (twice as long as other IUD products).[133] MIRENA® has carved out a market niche as the long-acting IUD.

On December 4, 2015, Bayer HealthCare filed a citizen petition with the FDA.[134] Of note, this petition was filed *one day before* the only patent protecting the drug was set to expire on December 5, 2015.

As of the date of this article, the FDA had yet to offer a substantive response to the concerns in the petition. In fact, by late-summer 2016, at least 260 days had passed since Bayer filed the petition. This is more than 100 days *beyond* the required 150-day response time mandated by FDAAA.[135]

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[131] Another potential aspect of serial petitions occurs when a petitioner requests numerous actions. For example, in 2015, Celgene petitioned the FDA to take particular action with regards to future ANDAs referencing ABRAXANE®, as well as to set "stringent" standards for oncology therapies using nanotechnology. Citizen Petition, Docket No. FDA-2015-P-0732 (filed Mar. 9, 2015). This petition was 80 pages in length and raises more issues than a mere request to impose additional bioequivalence testing. As of August 3, 2016, the FDA had not issued a final determination on this petition—more than *500 days* since the petition's filing.

[132] *See supra* Section IV.C.

[133] *Mirena*, DRUGS.COM, https://www.drugs.com/pro/mirena.html.

[134] Citizen Petition, Docket No. FDA-2015-P-4600 (filed on Dec. 4, 2015).

[135] While the FDA is required under the FDAAA to respond within 150 days unless delay would be necessary to protect the public health, there do not seem to be any measures by which this timeframe can be enforced. The FDA's failure to meet the 150-day period undermines Congress's intent.

Given that there is little public information on generics in the pipeline, we cannot decipher the complete strategy behind the filing of the MIRENA® petition. But at a minimum, the fact that the petition was filed *one day* before expiration of the only patent protecting the drug suggests that the company was interested in extending its exclusivity and ensuring that generics would be blocked from entering the market.[136]

C. DORYX®: Combination of Citizen Petitions and Product Hopping

Another concerning example is the use of citizen petitions in conjunction with product hopping. Petitions are a strong supplemental means to cause uncertainty and delay for generic companies. A recent product-hopping case sheds light on this dynamic.

Warner Chilcott[137] engaged in a decade-long effort to avoid direct competition with generic powerhouse, Mylan.[138] The product at issue, DORYX®, is used to treat acne. An immediate-release capsule version of the drug has been available since the 1960s.

In the late 1990s, Warner Chilcott began developing a delayed-release tablet version of DORYX® and received NDA approval in May 2005 for 75-mg and 100-mg unscored[139] tablets.

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[136] The suspicious timing of Bayer's petition regarding MIRENA® is not unique. For just a few other examples, see Citizen Petition, Docket No. FDA-2013-P-1508 (filed on Nov. 4, 2013) (OFIRMEV®, petition filed within 2 days of data exclusivity expiration); Citizen Petition, Docket No. FDA-2012-P-0943 (filed on Aug. 29, 2012) (LUNESTA®, petition filed within 1 day of nearest Orange Book listed patent); Citizen Petition, Docket No. FDA-2011-P-0823 (filed on Nov. 14, 2011) (CRESTOR®, petition filed within 8 days of nearest data exclusivity date).

[137] Warner Chilcott marketed the drug in the United States along with Mayne Pharmaceuticals. We refer solely to Warner Chilcott (which has now been absorbed by Actavis).

[138] For a complete recitation of the facts regarding the DORYX® product-hopping case see Mylan v. Warner Chilcott, Civ. No. 12-3824, 2015 WL 1736957 (E.D. Pa. Apr. 16, 2015), *appeal docketed* (3d Cir. May 20, 2015) (No. 15-2236).

[139] "Unscored" means there is no notch in the tablet to make it easier for a patient to split the tablet. For example, if a patient is prescribed two daily doses of 50 mg, then the patient can split a single-scored 100-mg tablet.

One year later, Mylan began developing generic 75-mg and 100-mg unscored tablets. Over the next seven years, Warner obtained various FDA approvals for tablets ranging from 75 mg to 150 mg, including single- and dual-scores. Each time Warner Chilcott received a new approval status for a different dosage and scored version of the tablet, Mylan sought to develop a generic.[140]

In January 2009, Warner Chilcott began to aggressively market a 150-mg, single-scored DORYX® tablet. Within a few months, this version of the tablet represented 71% of new DORYX® prescriptions. One year later, 90% of patients had been switched to this version. In the meantime, beginning in March 2010, Warner Chilcott began to develop a 150-mg, *dual*-scored version of the tablet. In June 2011, the FDA approved Mylan's generic 150-mg, single-scored version. Mylan had filed this ANDA almost three years earlier, in December 2008. Four months later, in September 2011, Warner Chilcott received FDA approval for its 150-mg, *dual*-scored version and immediately began to market that version.

This is where the citizen petition comes in. After Mylan received tentative approval for a generic, single-scored version of DORYX® in June 2011, a 505(q) citizen petition soon followed. Filed on September 23, 2011—before Mylan ever entered the market—Warner Chilcott's citizen petition urged the FDA to refrain from granting any ANDA referencing its 150-mg DORYX® tablet unless the proposed generic was a dual-scored version.[141] Warner Chilcott argued that patients would be confused if both single- and dual-scored 150 mg tablets were available.

The FDA denied this petition 138 days later on February 8, 2012. On that *same day*, the FDA gave final approval to Mylan's

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[140] Mylan's ability to rapidly develop new generic versions was important to its product line given Warner Chilcott's lifecycle management strategies. For example, Warner Chilcott announced that, as of May 2010, 90% of the DORYX® market had been transferred to 150-mg, single-scored tablets. This is important because the FDA would approve 75-mg and 100-mg unscored generic tablets in late 2010. In other words, whenever a generic version of DORYX® was ready for entry, Warner Chilcott was able to avoid direct competition by modifying its prior tablet version and obtaining approval before such generic entry.

[141] Citizen Petition, Docket No. FDA-2011-P-0702 (filed on Sept. 23, 2011).

ANDA for a 150-mg, single-scored tablet and granted it an AB-rating for Warner Chilcott's dual-scored version. Mylan launched its generic 150-mg, single-scored version immediately thereafter. This chronology strongly suggests that market entry of a single-scored, 150-mg generic was delayed approximately 138 days and was dependent on the FDA's resolution of Warner Chilcott's citizen petition.

The DORYX® saga presents a vivid case of how a citizen petition can be used to supplement other lifecycle management strategies, including product hopping. Although Warner Chilcott avoided direct generic competition by changing dosage forms and tablet scoring, the use of the citizen petition was able to delay generic entry by more than four months.

D. EpiPen®: Citizen Petitions, Settlements, & Price Hikes

Mylan's billion-dollar EpiPen® presents the final concerning example of citizen petitions.[142] Initially approved in 1987, EpiPen® auto-injectors are the primary means of treating severe allergic reactions.[143] Mylan received significant unwanted attention in 2016 for its price hike for EpiPen®,[144] but its citizen petition escaped notice. The lifecycle of EpiPen® reveals how Mylan used citizen petitions along with settlements to delay generic entry.

The saga began with Teva filing an ANDA seeking approval to market a generic EpiPen®.[145] Mylan commenced litigation against Teva, and the parties settled in April 2012. Under the terms of the settlement, Teva agreed to delay the launch of its generic

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[142] *Mylan sales and revenue up while EpiPen becomes its first $1 billion-selling product*, THE PHARMLETTER (Mar. 3, 2015), http://www.thepharmaletter.com/article/mylan-sales-and-revenue-up-while-epipen-becomes-its-first-1-billion-selling-product.

[143] *EpiPen*, DRUGS.COM (last visited Aug. 28, 2016), https://www.drugs.com/pro/epipen.html.

[144] *E.g.*, Andrew Pollack, *Mylan Raised EpiPen's Price Before the Expected Arrival of a Generic*, N.Y. TIMES B1 (Aug. 24, 2016); Olga Khazan, *Have You Ever Tried to Buy an EpiPen?* THE ATLANTIC (Aug. 24, 2016), http://www.theatlantic.com/health/archive/2016/08/epi-pens/497126/.

[145] The following facts are taken from Complaint, *King Pharma. Inc. v. Teva Parenteral Med. Inc.*, No. 09-652-GMS (D. Del. Aug. 28, 2009).

epinephrine auto-injector for more than three years, until June 2015.[146]

But as Teva's entry loomed, Mylan reached into its toolkit to pull out a citizen petition, which it filed on January 16, 2015, a mere six months before Teva was scheduled (pursuant to the settlement) to enter the market.[147] In its petition, Mylan contended that Teva should be required to demonstrate that its product was the "same as" Mylan's EpiPen®.[148] In other words, even though the parties had already agreed through settlement to delay Teva's generic entry for more than three years, Mylan sought to *further* delay the entry of Teva's generic through its citizen petition.

In addition to its January 2015 petition, the company waited almost *five months* after filing and only weeks before the FDA was required to respond, until May 2015, to supplement its petition with a 48-page independent study purportedly showing that patients would not use Teva's generic product correctly.[149]

Given that Teva's generic product had been in development for at least *six years* before the petition's filing, this late-filing of a supplemental study implicates significant timing questions. Why would such a study be submitted only weeks before the FDA was required to respond under the FDAAA's 150-day clock?

Even though Teva's ANDA ultimately was denied in the spring of 2016, Mylan may have sought, as noted above,[150] a simultaneous FDA resolution of a citizen petition and approval of a

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[146] *Mylan and Pfizer Announce Epinephrine Auto-injector Settlement Agreement with Teva*, Mylan (Apr. 26, 2012), http://newsroom.mylan.com/press-releases?item=123144. For more context, see Phil Milford, *Mylan, Pfizer Reach Epinephrine-Pen Settlement with Teva*, BLOOMBERG TECH. (Apr. 26, 2012), http://www.bloomberg.com/news/articles/2012-04-26/mylan-pfizer-announce-epinephrine-pen-settlement-with-teva-1-.

[147] Citizen Petition, Docket No. FDA-2015-P-0181 (filed on Jan. 16, 2015).

[148] *Id.*

[149] Supplement from Mylan Specialty Tab 1 IAA Handling Study Nonconfidential, Docket No. FDA-2015-P-0181 (posted May 5 and 28, 2015).

[150] *See supra* Section IV.D.

targeted ANDA. The late filing of supplemental information could well have been used to delay generic approval.

CONCLUSION

Citizen petitions have received far less attention than other conduct in the pharmaceutical industry. But they can play a crucial role in delaying generic entry. Brand firms file 92% of 505(q) citizen petitions, with the FDA denying more than 9 out of every 10 petitions.

We posited some reasons for the high denial rate, focusing on the increasing length of petitions, close proximity between petitions and expiration of a patent or FDA exclusivity, and the incidence of the FDA granting generic approval simultaneously with its resolution of petitions. These settings result in grants of only 3%, 2%, and 0%, respectively.

In short, and in defiance of Congress's attempt to limit abuse, citizen petitions continue to play an increasingly important role in delaying generic competition.