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

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Keywords

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LEAD ARTICLE

CITIZEN PETITIONS: LONG, LATE-FILED, AND AT-LAST DENIED

MICHAEL A. CARRIER AND CARL MINNITI*

The pharmaceutical industry is ground zero for many of the most challenging issues at the intersection of antitrust and intellectual property 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 filed 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, and (6) occasions in which the FDA approved generics on the same day it decided petitions.

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The study finds that brand firms filed 92% of 505(q) petitions. And it concludes that the FDA granted 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, with almost all of these petitions denied. Third, the FDA resolved a number of petitions on the same day it approved the generic, suggesting that the Agency delayed generic approval until it resolved the petition. These three settings resulted 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 a brand firm's toolkit of entry-delaying activity that can lead to consumers paying 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 law. Patents play a crucial role in the costly and lengthy process of new drug development. But the complexity of the regulatory regime and the dramatic effects on a brand firm’s 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.¹ 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.²

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 firms’ 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 concerns about the abuse of these petitions when it passed the Food and Drug Administration Amendments Act of 2007

1. *FTC v. Actavis, Inc.*, 133 S. Ct. 2223 (2013).
2. *New York ex rel. Schneiderman v. Actavis PLC (Namenda)*, 787 F.3d 638 (2d Cir. 2015).

(FDAAA),³ requiring the FDA to resolve citizen petitions in an expedient manner to avoid generic delay.⁴

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 filed the petitions, (3) the success rate of the petitions, (4) the petitions' length, (5) whether petitions were filed immediately before the expiration of a patent or data exclusivity, 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 ago⁵—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 page length longer than 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 brand petitions were filed within six months of the expiration of a patent or FDA exclusivity. 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.

This Article concludes by offering four case studies of concerning petitions. COPAXONE presents an instance of serial petitions, with Teva Pharmaceutical Industries (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

3. Pub. L. No. 110-85, 121 Stat. 823 (2007).

4. See 153 CONG. REC. 25,047 (2007) (statement of Sen. Hatch); see also CTR. FOR DRUG EVALUATION & RESEARCH, U.S. DEP'T OF HEALTH & 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 (1st rev. 2014) [hereinafter GUIDANCE FOR INDUSTRY].

5. See Michael A. Carrier & Daryl Wander, *Citizen Petitions: An Empirical Study*, 34 CARDOZO L. REV. 249 (2012).

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 anaphylaxis-treating EpiPen reveals the combination of petitions and settlements.

Part I of this Article introduces the Hatch-Waxman Act,⁶ enacted by Congress in 1984 to create a framework for brand and generic pharmaceutical competition. Part I also discusses settlements between brand and generic firms as well as product hopping, paying particular attention to the importance of generic competition and timing of generic entry.

Part II explains our methodology. It offers our general approach, describing our process for tracking petitions and explaining how we narrowed our analysis to a particular category of petitions. It also explains how we parsed "mixed" decisions to determine if the petitions were essentially granted or denied. And it presents our methods of analyzing issues related to the complexity and timing of the petitions.

Part III turns to citizen petitions, providing an introduction to the conduct and showing how they are filed most frequently in the pharmaceutical industry. This Part focuses on 505(q) petitions, which ask the FDA to take specific action against a pending generic drug application and which arose out of legislation enacted in 2007 to prevent market entry delays resulting from the filing of 505(q) petitions.

Part IV analyzes 505(q) petitions as well as their grant/denial rate both in general and for brand petitions in particular.

Part V then explores reasons for 505(q) petitions' low success rates. It traces the increasing complexity of petitions, the number of petitions 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 scenarios, Part V compares these specific grant/denial rates to the overall figures.

Finally, Part VI offers examples of concerning behavior of brand firms in filing serial petitions, late-filed petitions, and the combination of citizen petitions with product hopping and settlements. This Article concludes that citizen petitions represent a hidden tool in a brand firm's toolkit of entry-delaying activity that can

6. 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 (2012 & Supp. II 2015)).

lead to consumers paying high drug prices while providing no offsetting safety benefit.

I. PHARMACEUTICAL COMPETITION

The regulatory regime and economics of the pharmaceutical industry explain why it is uniquely susceptible to behavior delaying competitors' entry. Monopoly profits fall dramatically when generics enter the market, and the Hatch-Waxman Act and state substitution laws have created opportunities that can be exploited to forestall entry. It is in this setting that citizen petitions take their place along other, more well-studied behavior such as settlements and product hopping.⁷

A. *The 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.⁸ Generic drugs have the same active ingredients, dosage, administration, performance, and safety as patented brand drugs.⁹ 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.¹⁰ The FDA approval process took several years, and because the required tests constituted infringement of the brand firm's patent covering the drug, generic firms could not begin the process during the patent term.¹¹ 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

7. Portions of this Section are adapted from Carrier & Wander, *supra* note 5.

8. 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).

9. *Understanding Generic Drugs*, FDA, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/> (last updated Oct. 17, 2016).

10. Before Hatch-Waxman was enacted, some generic firms were able to either file "paper NDAs," use the antiquated Abbreviated New Drug Application 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 US Prior to the Hatch-Waxman Act*, REG. FOCUS, Sept. 2008, at 50.

11. CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 38 (1998) [hereinafter CBO STUDY], <https://www.cbo.gov/sites/default/files/105th-congress-1997-1998/reports/pharm.pdf>.

Congress enacted the Hatch-Waxman Act, there were no generic equivalents for roughly 150 drugs whose patent term had lapsed.¹²

Congress employed several mechanisms in the Act to promote generic competition. First, the Act allowed generic firms to experiment on drugs during their patent terms.¹³ Second, the Act created a new process for generics to obtain FDA approval, recognizing a new type of drug application, called an Abbreviated New Drug Application (ANDA). ANDAs allow generics to rely on brand firms' safety and efficacy studies, dispensing with the need for generics to conduct their own lengthy and expensive studies.¹⁴ Finally, the Hatch-Waxman Act granted 180 days of marketing exclusivity to the first generic to challenge the validity of a brand firm's patent or claim that the generic did not infringe the patent.¹⁵

B. Generic Entry

The Hatch-Waxman Act has been successful in increasing generic entry, with generic penetration rising from 19% of all prescriptions in 1984¹⁶ to 88% as of 2014.¹⁷ For the most popular drugs with expired patents, the share facing generic competition burgeoned from 35% in 1983 to almost 100% today.¹⁸

Generic entry is a pivotal event in a drug's lifecycle. When generics enter the market, prices can fall dramatically. The first generic entrant prices its product, on average, 5% to 25% lower than the

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

13. 35 U.S.C. § 271(e)(1) (2012) (exempting from infringement the manufacture, use, or sale of a patented invention for uses "reasonably related to the development and submission of information under a Federal law" regulating the manufacture, use, or sale of drugs).

14. See FTC, *GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 5* (2002), https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf (describing the ANDA procedure). 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. See *New Drugs*, 34 Fed. Reg. 2645, 2673 (Feb. 27, 1969) (discussing the creation of the previous ANDA system).

15. 21 U.S.C. § 355(j)(2)(A)(vii)(IV), (j)(5)(B)(iv) (2012).

16. 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. 137 (2002) (statement of Gregory J. Glover, Pharmaceutical Research and Manufacturers of America).

17. GENERIC PHARM. ASS'N, *GENERIC DRUG SAVINGS IN THE U.S.* 1 (2015), http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf.

18. CBO STUDY, *supra* note 11, at 37.

brand drug.¹⁹ The presence of a second generic lowers the price to approximately half the brand price.²⁰ In markets in which six or more generics enter, the price falls to a quarter of the brand price.²¹ One survey showed that patients could save 52% in the daily costs of their medications by purchasing generic drugs.²² In fact, even though generics make up 80% of prescriptions, they amount to only 28% of drug costs.²³

In addition, generic drugs quickly take sales from brand drugs. Once a generic enters the market, the brand product loses 44% to 90% of its market share within the first twelve months.²⁴ 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.²⁵

These trends are amplified by health insurance providers' encouragement or requirement of generic drugs.²⁶ All states either allow or require pharmacists who receive prescriptions for brand drugs to substitute generics.²⁷ Medicaid policies and managed-care plans also encourage substitution.²⁸

19. *Id.* at xiii; *Generic Competition and Drug Prices*, FDA, <http://www.fda.gov/About/fda/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm> (last updated May 13, 2015).

20. *Generic Competition and Drug Prices*, *supra* note 19.

21. *Id.*

22. *Savings from Generic Drugs Purchased at Retail Pharmacies*, FDA, <http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm134205.htm> (last updated May 6, 2016).

23. GENERIC PHARM. ASS'N, *supra* note 17, at 1.

24. FTC, PAY-FOR-DELAY: HOW DRUG COMPANY PAY-OFFS COST CONSUMERS BILLIONS 8 (2010), <http://www.ftc.gov/os/2010/01/100112payfordelayrpt.pdf>; CBO STUDY, *supra* note 11, at xiii; *see also* DOUG LONG, IMS HEALTH, 2003 YEAR IN REVIEW: TRENDS, ISSUES, FORECASTS 35 (2004), <http://www.piapr.org/index.php?src=documents&srctype=download&id=38> (providing an overview of generic drug market share after first thirteen weeks on the market); Atanu Saha et al., *Generic Competition in the US Pharmaceutical Industry*, 13 INT'L J. ECON. BUS. 15, 29-31 (2006) (examining generic drug market share after several months on the market).

25. *See* Fiona M. Scott Morton, *Barriers to Entry, Brand Advertising, and Generic Entry in the US Pharmaceutical Industry*, 18 INT'L J. INDUS. ORG. 1085, 1102 (2000) (analyzing the characteristics of a drug market and how those characteristics predict generic drug market entry success); Saha et al., *supra* note 24, at 27 (emphasizing that the size of a brand firm's drug market, including extremely successful "blockbuster" drugs, is key in determining generic drug success).

26. 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).

27. *See id.* at 23-24 (emphasizing that when a state's policies and laws permit a pharmacist to substitute a generic for a brand firm drug, generic penetration

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

C. Conduct Delaying Generic Entry

Because of the dramatic effects of generic competition, brand firms have used an array of tactics to delay generic entry. One activity involves patent litigation settlements in which a brand pays a generic to settle its 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. In particular, brand firms have paid generic firms to delay entering the market, a practice the Supreme Court held could have "significant adverse effects on competition" and violate the antitrust laws.²⁹ 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.³⁰ 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, have switched from a capsule to a tablet—or vice versa—or from either of these forms to an extended-release drug or chewable tablet.³¹ Much of this product hopping activity has been successful because it has avoided the effect of state drug product substitution (DPS) laws,³² in effect in all fifty states today, which allow or require pharmacists—absent a doctor's contrary instructions—to substitute generic versions of brand-name prescriptions.³³ These

increases rapidly); Aaron S. Kesselheim & Jonathan J. Darrow, *Hatch-Waxman Turns 30: Do We Need a Re-Designed Approach for the Modern Era?*, 15 YALE J. HEALTH POL'Y L. & ETHICS 293, 312 (2015); see *infra* text accompanying notes 32–33.

28. See *In re Schering-Plough Corp.*, 136 F.T.C. 956, 979 n.37 (2003), *vacated*, 402 F.3d 1056 (11th Cir. 2005).

29. *FTC v. Actavis, Inc.*, 133 S. Ct. 2223, 2231 (2013).

30. Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV. 7, 15 (2014).

31. E.g., Steve D. Shadowen et al., *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 RUTGERS L.J. 1, 3, 31–32 (2009).

32. *Id.* at 13–18.

33. Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1017–19 (2010).

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 the generic is not equivalent to the new brand version.³⁴

A central issue in both settlements and product hopping involves timing. Product hopping is most successful when brand firms not only can avoid state DPS laws but also can switch the market before generic entry. Brand firms often stop promoting the old version of the drug, switching their marketing to the new product and offering the “uncontested message” of the new product’s superiority.³⁵ Patients who switch to the new drug are unlikely to switch back.³⁶

Brand 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, protecting their monopoly on the original drug. The value of this combination is that a settlement that prevents patent challenges for a period of time—even less than the duration of the patent—allows the brand firm to switch the market to the new product. So by the time the generic enters years later, the market will have already migrated to the new product. As a result, the generic firm, which can no longer take advantage of state DPS laws, fails to provide meaningful downward pressure on the brand firm’s new drug price.

Brand firms’ 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 are able to buy additional time in which to delay generic entry. This Article evaluates citizen petitions, presenting original data on how they are being used today. The necessary first step of such analysis is a discussion of how we conducted our study.

II. METHODOLOGY

This Part explains our methodology. Section A offers our general approach, describing our process for tracking petitions and explaining how we narrowed our analysis to a particular category of petitions. Section B explains how we parsed “mixed” decisions, which grant in part and deny in part the petition, to determine if the petitions were essentially granted or denied. Section C then presents

34. Shadowen et al., *supra* note 31, at 5.

35. *Id.* at 51.

36. *Id.* at 51–55.

our methods of analyzing issues related to the complexity and timing of the petitions.

A. General

We tracked citizen petitions by using the industry-standard compilation available at FDA Law Blog.³⁷ This website maintains an ongoing record of petitions filed with the FDA. Known as the FDA Citizen Petition Tracker,³⁸ 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 2011³⁹ and continue through 2015, the last full year for which citizen petition information is available.

Within this timeframe, we focused on petitions in the "Drug" category.⁴⁰ And within this category, we limited our analysis to "505(q) petitions."⁴¹ As described in more detail below,⁴² these

37. Hyman, Phelps & McNamara, P.C., FDA LAW BLOG, <http://www.FDALawblog.net/> (last visited Nov. 30, 2016).

38. The Tracker includes the following data: Docket Number, Petitioner, Product Name/Issue, Category, Petition Type, Receipt Date, Decision Date, and Decision. See FDA Citizen Petition Tracker, FDA LAW BLOG, www.fdalawblog.net/FDA_law_blog_hyman_phelps/files/CPTracker.xls (last updated Nov. 4, 2016). As of August 2, 2016, 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. See *id.*

39. See Carrier & Wander, *supra* note 5, at 249 (reviewing citizen petitions filed between 2001 and 2010).

40. 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." See FDA Citizen Petition Tracker, *supra* note 38.

41. 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." See, e.g., Endo Pharmaceuticals Inc. Citizen Petition, No. FDA-2012-P-0895-0001 (Aug. 13, 2012), <https://www.regulations.gov/document?D=FDA-2012-P-0895-0001>. Second, we excluded the two petitions that were withdrawn within 7 days and refiled. See Pfizer, Inc. Citizen Petition, No. FDA-2012-P-0545-0001 (May 31, 2012) (petition aimed at LYRICA generic withdrawn 7 days later and refiled on June 6, 2012); Navinta LLC Citizen Petition, No. FDA-2011-P-0072-0001 (Feb. 8, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0702-0001> (petition aimed at Venofer generic withdrawn 2 days later and refiled on Feb. 10, 2011).

In contrast, we included the six petitions for which withdrawal occurred more than 7 days after the filing. For example, on July 16, 2012, Purdue Pharmaceuticals filed a petition aimed at a generic version of OxyContin. Purdue Pharma LP Citizen Petition 1, No. FDA-2012-P-0760-0001 (July 16, 2012) [hereinafter Purdue Pharma Citizen Petition 1], <https://www.regulations.gov/document?D=FDA-2012-P-0760-0001>. This petition was withdrawn 79 days later, on October 3, 2012, because Purdue

petitions were created to ensure that citizen petitions would not be abused to delay generic entry. Other types of petitions, such as ANDA Suitability and reference listed drug (RLD) designation petitions, do not immediately pose such a threat and therefore fall outside the scope of this study.

B. *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. Continuing the project we began in our previous article, we analyzed the mixed decisions from the petitions received by the FDA between 2011 and 2015 to determine which of the mixed decisions were essentially granted and which were essentially denied.

had filed another petition in late August on the same subject matter. Purdue Pharma L.P. Citizen Petition 2, No. FDA-2012-P-0939-0001 (Aug. 29, 2012) [hereinafter Purdue Pharma Citizen Petition 2], <https://www.regulations.gov/document?D=FDA-2012-P-0939-0001>. This petition is worthy of attention because 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. *See id.* 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. *See* Purdue Pharma Citizen Petition 1, *supra*. 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. *See* Purdue Pharma Citizen Petition 2, *supra*. 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 7 days after filing raised similar concerns, and we included them in our dataset. *See* Duchesnay Citizen Petition, No. FDA-2014-P-1302-0001 (July 11, 2014) (petition aimed at DICLEGLIS withdrawn after 70 days); SigmaPharm Laboratories, LLC Citizen Petition, No. FDA-2013-P-1399-0001 (Oct. 31, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1399-0001> (petition aimed at SAPHRIS withdrawn after 27 days and immediately refilled); Teva Pharmaceutical Industries Ltd. Citizen Petition, No. FDA-2013-P-1128-0001 (Sept. 12, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1128-0001> (petition aimed at COPAXONE withdrawn after 113 days); Horizon Pharma, Inc. Citizen Petition, No. FDA-2013-P-1082-0001 (Sept. 4, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1082-0001> (petition aimed at RAYOS withdrawn after 30 days); Janssen Pharmaceuticals, Inc. Citizen Petition, No. FDA-2012-P-0295-0001 (Mar. 26, 2012), <https://www.regulations.gov/document?D=FDA-2012-P-0295-0001> (petition aimed at ELMIRON withdrawn after 184 days).

42. *See infra* notes 81–92 and accompanying text.

We found that between 2011 and 2015, the FDA issued 23 mixed petitions. Based on a thorough review, we concluded that, of this group, the FDA essentially granted 6 petitions and essentially denied 17.⁴³

1. *Essential denials*

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 Pharmaceutica

43. The following are the 23 mixed petitions and our characterization:

<i>Petition</i>	<i>Decision Date</i>	<i>Decision</i>
FDA-2011-P-0127	June 7, 2011	Essentially Granted
FDA-2011-P-0433	Nov. 21, 2011	Essentially Granted
FDA-2011-P-0610	July 23, 2014	Essentially Denied
FDA-2011-P-0767	Apr. 17, 2012	Essentially Granted
FDA-2012-P-0583	Nov. 30, 2012	Essentially Denied
FDA-2012-P-0932	Jan. 23, 2013	Essentially Denied
FDA-2012-P-1087	Mar. 22, 2013	Essentially Denied
FDA-2012-P-1091	Mar. 29, 2013	Essentially Denied
FDA-2013-P-0127	Dec. 11, 2014	Essentially Denied
FDA-2013-P-0371	July 23, 2014	Essentially Denied
FDA-2013-P-0371	Feb. 9, 2015	Essentially Denied
FDA-2013-P-0572	Oct. 7, 2013	Essentially Denied
FDA-2013-P-0664	Oct. 30, 2015	Essentially Granted
FDA-2013-P-0703	Oct. 25, 2013	Essentially Denied
FDA-2013-P-0850	Dec. 19, 2013	Essentially Denied
FDA-2013-P-0995	Sept. 8, 2013	Essentially Granted
FDA-2013-P-1283	Mar. 12, 2014	Essentially Denied
FDA-2013-P-1505	Apr. 10, 2014	Essentially Denied
FDA-2014-P-0304	Nov. 20, 2014	Essentially Denied
FDA-2014-P-0404	Aug. 29, 2014	Essentially Denied
FDA-2014-P-1269	Sept. 14, 2015	Essentially Granted
FDA-2015-P-0065	Feb. 10, 2016	Essentially Denied
FDA-2015-P-1404	Feb. 10, 2016	Essentially Denied

LLC's and Allergan, Inc.'s separate petitions regarding the multi-billion dollar immunosuppressant, RESTASIS.⁴⁴ The companies petitioned 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 45-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 testing.⁴⁵ And it "determined that [the FDA] has clear legal authority to receive and approve an ANDA for cyclosporine ophthalmic emulsion that relies on" the testing in its bioequivalence guidelines.⁴⁶

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 requests to disclose the in vitro bioequivalence methods the FDA intended to apply to ANDAs referencing RESTASIS and to not approve or receive any ANDA referencing RESTASIS unless FDA first responded to a specific test conducted by RESTASIS' sponsor, Allergan.⁴⁷ This petition only sought 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.⁴⁸ 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.

44. See Physical Pharmaceutica LLC Citizen Petition, No. FDA-2015-P-1404-0001 (Apr. 24, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1404-0001>; Allergan, Inc. Citizen Petition, No. FDA-2014-P-0304 (Feb. 28, 2014).

45. FDA Combined Response to Physical Pharmaceutica LLC and Allergan, Inc. Citizen Petitions, FDA, No. FDA 2015-P-1404-0007, at 44 (Feb. 10, 2016), <https://www.regulations.gov/document?D=FDA-2015-P-1404-0007>.

46. *Id.*

47. *Id.*

48. Abbott Laboratories Citizen Petition, No. FDA-2011-P-0610-0001 (Aug. 19, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0610-0001>.

The FDA denied Abbott's request on the grounds that "additional notice-and-comment rulemaking to revisit [the FDA's] long-established approach to TE ratings is not necessary or appropriate."⁴⁹ The agency also denied Abbott's lengthy requests for reevaluation of other companies' topical testosterone gel interchangeability status or labels.⁵⁰

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."⁵¹ 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.

2. *Essential grants*

In other instances, the FDA "essentially grants" petitions that raise safety issues. For example, on May 31, 2011, Lehigh Valley Technologies, Inc. (Lehigh) and Glenmark Generics, Inc. (Glenmark) jointly filed a petition regarding oxycodone HCl pain relievers, such as OxyContin, Roxicodone, and Oxecta.⁵² The petitioners requested that the FDA refrain from approving any ANDA or new drug application (NDA) for a single entity oxycodone hydrochloride unless the active pharmaceutical ingredient ("API") satisfied certain impurity limits.⁵³ The petitioners also requested that the API meet these specific impurity limits "under accelerated stability conditions for [six] 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.⁵⁴

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. Because the Agency had been

49. FDA Response to Abbott Laboratories Citizen Petition, FDA, No. FDA-2011-P-0610-0010, at 11, 18 (July 23, 2014), <https://www.regulations.gov/document?D=FDA-2011-P-0610-0010>.

50. *See id.* at 23–24, 28–29, 32, 33.

51. *Id.* at 33.

52. FDA Response to Lehigh and Glenmark Citizen Petition, FDA, No. FDA-2011-P-0433-0005, at 1 (Nov. 21, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0433-0005>.

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

54. *Id.*

working on decreasing impurity levels since 2002, the petitioners' request to require any oxycodone HCl products to establish specific impurity limits or submit toxicology studies confirming impurities would not be expected to cause cancer or genetic mutations was granted.⁵⁵

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."⁵⁶ 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.⁵⁷

We characterized this petition as "essentially granted" because the FDA agreed with the petitioners that the ANDA applicant must establish certain impurity limits before approval. The Agency agreed with the petitioners that "[i]t is in the interests of public health and consistent with current Agency policy that applicants for single-ingredient oxycodone HCl products meet this standard."⁵⁸ A complete list of our mixed decision judgments can be found in footnote 43.

C. Complexity & Timing

In addition to mixed decisions, the data we present in Part V calls for an additional discussion of methodology. Once we narrowed 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 brand product that was the 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 petitions by brand firms, the company typically notes that it is the holder of a particular NDA and asks the FDA to take a specific 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

55. *Id.* at 2.

56. *Id.* at 2, 8, 9.

57. *Id.* at 2, 10.

58. *Id.* at 2.

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 date⁵⁹ 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.

Third, we obtained information on any approved ANDA referencing the brand product at issue. Because a goal of our study was 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 tracked ANDA approval dates to determine how often the FDA resolved a petition on the same day—or in the same month—it approved the targeted ANDA. As we explain below,⁶⁰ this is important because same-day (or same-month) resolution raises the prospect of delayed ANDA approval.

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.⁶¹

59. 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. *See* 21 U.S.C. § 355(j)(5)(F)(ii) (2012). 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. *See id.* § 355(c)(3)(E)(iii).

60. *See infra* Section V.C.

61. For an example, consider the pain medication OFIRMEV. Cadence Pharmaceuticals filed a petition on November 4, 2013 regarding a prospective

Having narrowed the universe of petitions and obtained crucial data points, we found 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 has been used in the pharmaceutical regulatory regime.

A 6-month period mirrors the timeframe of 180 days within which—before being reduced to 150 days in the FDAAA—the FDA was required to 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.⁶² Finally, given that generic drugs typically take more than two years to develop and obtain FDA approval,⁶³ it is reasonable to assume that a petition filed within six months of an exclusionary date has the potential to affect a generic firm’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 reap 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 generic entry.

It goes without saying that patent protection and data exclusivity underpin a drug product’s lifecycle. We thus assume that the

ANDA. Cadence Pharmaceuticals, Inc. Citizen Petition, No. FDA-2013-P-1508-0001 (Nov. 4, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1508-0001>. 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. CTR. FOR DRUG EVALUATION & RESEARCH, FDA, APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (33d ed. 2013) [hereinafter ORANGE BOOK]. Listed under OFIRMEV were two U.S. Patents: U.S. Patent Nos. 6,028,222 (“the ’222 Patent”) and 6,992,218 (“the ’218 Patent”) expiring on August 5, 2017 and June 6, 2021, respectively. *Id.* at ADA 1. Also listed under the new product code (“NP”) was an exclusivity of November 2, 2013. *Id.* So at the time Cadence filed the petition on November 4, 2013, the ’222 Patent was set to expire in 1370 days and the ’218 Patent was set to expire in 2771 days. While these expiration dates were far removed, the sole exclusivity listed under code NP had expired only 2 days before Cadence filed the petition.

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

63. See Carrier, *supra* note 33, at 1018 (explaining that generic firms experience delays due to brands’ reformulation, patent litigation, and FDA approval of generics’ reformulation).

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.⁶⁴ 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 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. Although 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 of 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 took a simple approach to the issue. If a petition is filed within six months of an exclusionary date, we treated that date as being noteworthy. Rather than selecting among potential exclusionary dates, we used the actions of the brand—which would be aware of the approaching expirations—to determine the relevant dates. And as we show in finding that the FDA denies 98% of late-filed petitions,⁶⁵ the broad universe of exclusionary dates seems to be accompanied by petitions filed more to delay generic entry than to obtain success on the merits.

64. See *supra* notes 19–21 and accompanying text.

65. See *infra* note 135 and accompanying text.

III. CITIZEN PETITIONS: OVERVIEW

Having explained our methodology, we now provide a more robust background on citizen petitions, exploring the industries in which they are filed and different categories of petitions. We then discuss congressional reports on the topic before presenting the findings of our previous study on citizen petitions.

A. *Background on Citizen Petitions*

The First Amendment ensures that Congress cannot abridge “the right of the people . . . to petition the Government” to take a particular action.⁶⁶ In 1946, Congress extended this protection to rules created by administrative agencies by enacting the Administrative Procedure Act (APA),⁶⁷ which required government agencies to provide the public with the right to petition for the issuance, amendment, or repeal of an administrative rule.⁶⁸ In accordance with the APA, the FDA allows individuals to express safety, scientific, or legal issues regarding a product through citizen petitions.⁶⁹

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.”⁷⁰ All citizen petitions must include the “[a]ction requested,” particularly the “rule, order, or other administrative action” that the petitioner seeks to “issue, amend, or revoke.”⁷¹ Petitions also must disclose a “[s]tatement of grounds,” including “the factual and legal grounds on which the petitioner relies.”⁷²

66. 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 three paragraphs are adapted from Carrier & Wander, *supra* note 5, at 259–60.

67. Administrative Procedure Act of 1946, Pub. L. No. 79-404, 60 Stat. 237 (codified as amended at 5 U.S.C. §§ 551–59 (2012)).

68. 5 U.S.C. § 553(e); see also Stacey B. Lee, *Is a Cure on the Way?—The Bad Medicine of Generics, Citizen Petitions, and Noerr-Pennington Immunity*, 20 KAN. J.L. & PUB. POL’Y 98, 108–09 (2010).

69. 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*] (statement of Gary Buehler, Director, Office of Generic Drugs, FDA), <http://www.aging.senate.gov/imo/media/doc/hr161gb.pdf>; see also § 10.30(b)(B) (requiring petitions to state factual and legal grounds for requests).

70. 21 C.F.R. §§ 10.25, 10.30.

71. *Id.* § 10.30(b)(A); *Comment on Proposed Regulations and Submit Petitions*, FDA, <http://www.fda.gov/RegulatoryInformation/Dockets/Comments/default.htm> (last updated Oct. 20, 2014).

72. 21 C.F.R. § 10.30(b)(B).

Citizen petitions additionally must describe any environmental effects of the requested action.⁷³ And if requested by the Commissioner of Food and Drugs, they must address the petitions' economic impact, in particular, effects on "(1) [c]ost (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."⁷⁴

Some citizen petitions may raise valid safety concerns, but in many cases, they offer little 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)],"⁷⁵ 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.

73. *Id.* § 10.30(b)(C).

74. *Id.* § 10.30(b)(D).

75. *Generic Drug Maze Hearing*, *supra* note 69, at 14.

Table 1: Frequency of Citizen Petitions by Industry⁷⁶

<i>Industry</i>	<i>2013</i>	<i>2014</i>	<i>2015</i>
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, RLD designation petitions, discontinuation petitions, ANDA suitability petitions, and 505(q) certified petitions. Table 2 provides a breakdown of these different types.

76. As noted above, *see supra* note 40, 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.

Table 2: Frequency of Types of Drug Petitions

Type of Drug Petition	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.⁷⁷ *RLD designation petitions* ask that the FDA designate a particular approved drug as a reference listed drug for the purposes of filing an ANDA.⁷⁸ *Discontinuation petitions* require that the FDA confirm whether an approved drug product was taken off the market for safety or efficacy concerns.⁷⁹ *ANDA suitability petitions* ask that the FDA confirm whether a prospective generic application can consist of certain features.⁸⁰ *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.

77. *E.g.*, CUNY School of Public Health & Hunter College Citizen Petition, No. FDA-2015-P-1900-0001 (May 27, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1900-0001> (requesting that the FDA mandate certain label language for a contraception product).

78. *E.g.*, Lachman Consultant Services, Inc. Citizen Petition, No. FDA-2015-P-1899-0001 (May 27, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1899-0001>.

79. *E.g.*, Wiley Rein LLP Citizen Petition, No. FDA-2015-P-1752-0001 (May 15, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1752-0001>.

80. *E.g.*, Qilu Pharmaceutical Co. Citizen Petition, Docket No. FDA-2015-P-1590-0001 (May 7, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1590-0001> (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).

Section 505(q) appears in section 914 of the FDAAA.⁸¹ Congress intended for the section to reduce delays from petitions,⁸² with section 505(q) applying to “certain petitions that request that the [FDA] take any form of action related to a pending ANDA”⁸³ and requiring petitioners to certify that they did not delay in filing the petition.⁸⁴ The FDAAA mandated that the FDA take final action no later than 180 days—later shortened to 150 days⁸⁵—after the petition’s filing date unless delay would be necessary to protect the public health.

As shown below,⁸⁶ brand firms have filed the vast majority of 505(q) petitions. Petitions filed by brand firms have largely sought to require the generic firm 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 as the brand drug.⁸⁷

Generic firms also have filed 505(q) petitions. In one scenario, they have sought to mandate certain types of bioequivalence testing on other generic applications.⁸⁸ In another, first-filing generics have requested that the FDA not approve other ANDAs until the end of the 180-day exclusivity period.⁸⁹ In each of these cases, the FDA must respond to 505(q) petitions within 150 days of filing.⁹⁰

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

81. 21 U.S.C. § 355(q) (2012).

82. See 153 CONG. REC. 25,047 (2007) (statement of Sen. Hatch); GUIDANCE FOR INDUSTRY, *supra* note 4, at 3–4.

83. 21 U.S.C. § 355(q)(1)(H).

84. *Id.*

85. Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 1135, 126 Stat. 993, 1123 (2012) [hereinafter FDASIA].

86. See *infra* Section IV.A.

87. 21 U.S.C. § 355(j)(8)(B).

88. *E.g.*, Apotex Corp. Citizen Petition, No. FDA-2014-P-0099-0001 (Jan. 13, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-0099-0001> (requesting that the FDA reject new ANDAs unless their bioequivalence studies contained a “crossover design”).

89. *E.g.*, Sigmapharm Laboratories, LLC Citizen Petition, No. FDA-2013-P-1623-0001 (Dec. 9, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1623-0001> (petitioning the FDA not to approve other ANDAs for Asenapine Maleate Sublingual Tablets).

90. 21 U.S.C. § 355(q)(1)(F); see *supra* note 85 and accompanying text.

or regulatory concern.⁹¹ Despite denying nearly all petitions—as shown below⁹²—the FDA has never invoked this power.

B. Congressional Reports

The FDAAA mandates that the FDA submit annual reports to Congress summarizing trends and data on 505(q) petitions.⁹³ 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.⁹⁴ As of the date of this Article, eight reports have been submitted to Congress.

Employing a narrow definition of delay, the reports note that 9 petitions from fiscal years 2008 through 2015 have caused the FDA to delay generic approval.⁹⁵ According to the reports, these 9 petitions delayed the approval of 10 generic drug products. The amount of

91. 21 U.S.C. § 355(q)(1)(E).

92. *See infra* Section IV.B.

93. 21 U.S.C. § 355(q)(3).

94. *Id.*

95. *See* FDA, 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, at 1 (2016) [hereinafter FY 2015 REPORT]; FDA, REPORT TO CONGRESS: SEVENTH ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2014, at 1 (2015) [hereinafter FY 2014 REPORT]; FDA, 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, at 3 (2014) [hereinafter FY 2013 REPORT]; FDA, 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, at 3 (2013) [hereinafter FY 2012 REPORT]; FDA, 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, at 3 (2012) [hereinafter FY 2011 Report]; FDA, REPORT TO CONGRESS: THIRD ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2010, at 3 (2011) [hereinafter FY 2010 REPORT]; FDA, REPORT TO CONGRESS: SECOND ANNUAL REPORT ON DELAYS IN APPROVALS OF APPLICATIONS RELATED TO CITIZEN PETITIONS AND PETITIONS FOR STAY OF AGENCY ACTION FOR FISCAL YEAR 2009, at 3 (2010) [hereinafter FY 2009 REPORT]; FDA, 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, at 3 (2009) [hereinafter FY 2008 REPORT].

delay ranged from 9 days to 138 days.⁹⁶ 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) may not be discouraging the submission of petitions that are intended primarily to delay the approval of competing drug products and do not raise valid scientific issues.”⁹⁷ 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 an earlier study, the first empirical study of citizen petitions, one of us reviewed every petition filed with the FDA between 2001 and 2010.⁹⁸ We found that petitions increased through the decade, with a total of 258 petitions filed.⁹⁹ We observed that 68% of petitions were filed by brand firms, and that more than three-quarters of brand petitions targeted generic drugs.¹⁰⁰

We concluded that the FDA granted 19% of citizen petitions and denied 81%.¹⁰¹ Generic petitions were more successful, with 28% granted and 72% denied, than brand petitions, with 19% granted and 81% denied.¹⁰²

The 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 34.¹⁰³ Brand petitions against generics increased from 9 to 16 per year.¹⁰⁴ And the grant rate for brand petitions against generics declined from 20% to 19%.¹⁰⁵

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

96. FY 2013 REPORT, *supra* note 95, at 3 (25 days); FY 2011 REPORT, *supra* note 95, at 3 (78 days); FY 2010 REPORT, *supra* note 95, at 3 (9 days); FY 2009 REPORT, *supra* note 95, at 4 (27 days); FY 2008 REPORT, *supra* note 95, at 4 (138 days).

97. FY 2015 REPORT, *supra* note 95, at 8.

98. Carrier & Wander, *supra* note 5, at 249.

99. *Id.* at 270.

100. *Id.* at 270–71.

101. *Id.* at 274.

102. *Id.* at 275–76.

103. *Id.* at 282.

104. *Id.*

105. *Id.*

IV. GRANTS/DENIALS 2011–2015

This Part offers empirical research on the FDA's grants and denials of citizen petitions between 2011 and 2015. It begins by exploring the total number of 505(q) petitions. And it then surveys petitions' success rate in general and among brand firms in particular.

A. *Total 505(q) Petitions*

We begin with the total number of 505(q) citizen petitions filed each year from 2011 through 2015. Table 3¹⁰⁶ presents every petition labeled "Citizen Petition (505(q) Certification)" that appeared in the FDA Citizen Petition Tracker.¹⁰⁷ 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 filers.¹⁰⁸ 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 firm 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 concerns and lie outside the scope of this study.

The observation that brand firms file more than 9 out of 10 505(q) petitions raises concern. 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.¹⁰⁹

106. *Infra* note 110.

107. FDA Citizen Petition Tracker, *supra* note 38.

108. 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 76.

109. It is conceivable that interest groups and competing generic firms could file fewer 505(q) petitions as a result of filing petitions at other times. Filing petitions that challenge safety or efficacy at times when there is not a pending ANDA could potentially displace 505(q) petitions.

Table 3: 505(q) Petitions and Petitioners by Year¹¹⁰

Year	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%

B. Success Rate

Our previous study found that the FDA denied 81% of petitions, granting only 19%.¹¹¹ Remarkably, *the grant rate has fallen significantly, even from that low rate.* Between 2011 and 2015, the FDA issued 109 substantive decisions.¹¹² Table 4 shows that the FDA issued 3 outright grants and 83 outright denials. The remaining 23 decisions were mixed decisions.¹¹³

110. 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 41; *see also* Purdue Pharma Citizen Petition 2, *supra* note 41, at 1, 2 (showing the second of Purdue's two petitions, which is identical to the first petition except for its filing date and an updated 505(q) statement that targeted a generic version of OxyContin). 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.*, Novartis Citizen Petition, No. FDA-2013-P-0247-0001 (Mar. 4, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-0247-0001>; Novartis Supplement and Petition for Reconsideration, No. 2013-P-0247-0004 (Aug. 23, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-0247-0004>. As a result, in 2013, there were 32 petitioners and 37 petitions.

111. *See* Carrier & Wander, *supra* note 5, at 274 tbl.3.

112. While 124 505(q) petitions were filed between 2011 and 2015, the FDA issued only 109 substantive decisions during that period. *See supra* Table 3 (showing the number of petitions filed from 2011 to 2015); *infra* Table 4 (providing the total number of substantive decisions).

113. 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

Table 4: Success Rate of Citizen Petitions by Year¹¹⁴

<i>Year</i>	<i>Petitions Granted</i>	<i>Petitions Denied</i>	<i>Mixed</i>
2011	2	12	4
2012	1	19	4
2013	0	23	10
2014	0	17	4
2015	0	12	1
Total	3	83	23

The recoding of mixed decisions as essentially granted or denied underscores even more emphatically the low probability of success. As we showed above,¹¹⁵ careful analysis of the 23 mixed decisions reveals 6 essential grants and 17 essential denials.¹¹⁶ Incorporating these mixed decisions, there were a total of 9 grants and 100 denials.

Figure 1 presents these results graphically. From 2011 through 2015, the denial rate ranged between 72% and 100% each year. In fact, the denial rate increased markedly from 72% in 2011 to 96%, 94%, 95%, and 100% from 2012 to 2015. In these four years, there were only 1, 2, 1, and 0 petitions granted, respectively.¹¹⁷ In total, the FDA granted *only* 8% of 505(q) petitions, denying a full 92%.

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 68% 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.

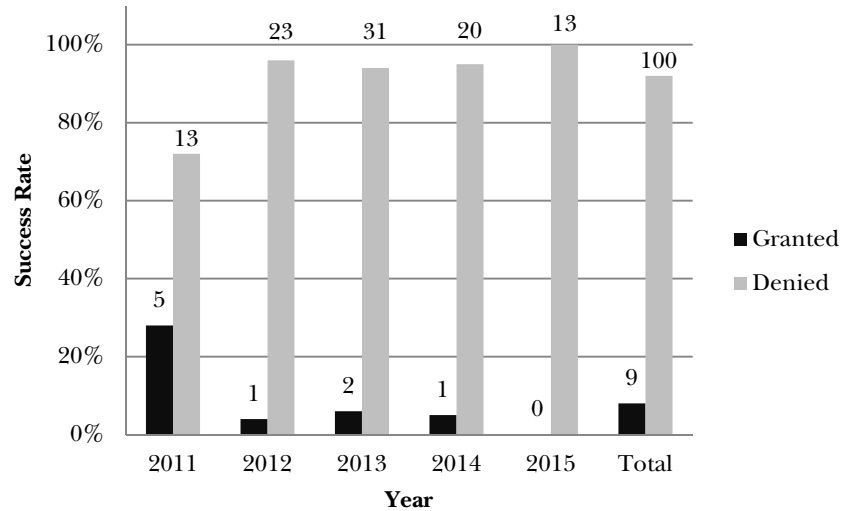
114. The number of denials and grants may differ from the number of petitions filed because the FDA may issue multiple decisions on a petition. *E.g.*, Auxilium Pharmaceuticals, Inc. Citizen Petition, No. FDA-2013-P-0371 (Mar. 26, 2013), <https://www.regulations.gov/docket?D=FDA-2013-P-0371> (including Auxilium's petition targeting testosterone gel Testim and both of FDA's mixed, "essentially denied" responses from July 23, 2014 and February 9, 2015).

115. *See supra* Section II.B.

116. *See supra* note 43 (providing conclusions on the 23 decisions).

117. *See supra* Table 4 and note 43. The categories "granted" and "denied" include mixed decisions that we determined to be essentially granted/denied. *See id.*

Figure 1: Success Rate of Citizen Petitions by Year¹¹⁸



C. 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 examined the success rate of petitions filed by a brand firm.

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—Figure 2 shows that 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. As a point of comparison, the previous study showed that from 2001 through 2010, the FDA granted 22 brand firm petitions (19%) while denying 96 (81%).¹¹⁹ Tracking the increased number of total 505(q) denials in the past five years,¹²⁰ the brand firm success rate of 9% is roughly half of what it was in the previous decade. In particular, the brand success rates from 2011 through 2015 were

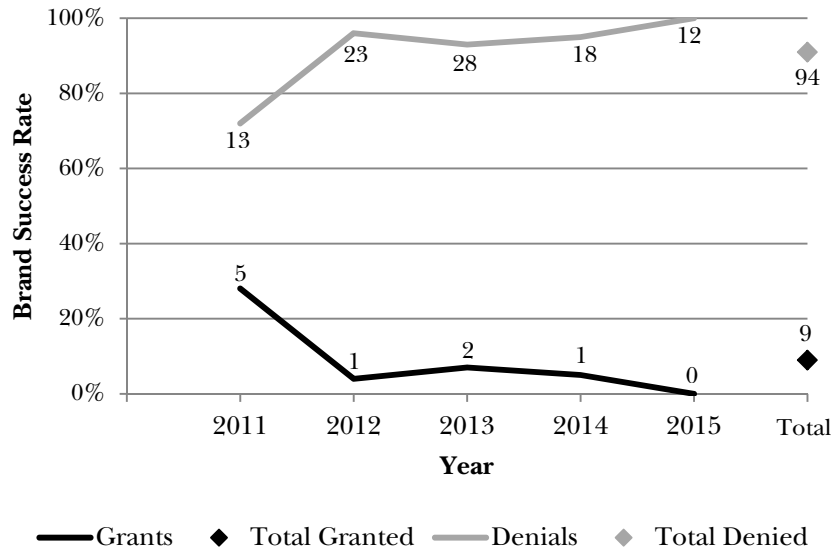
118. See *supra* Table 4 for figures on grants and denials and note 43 for mixed decisions.

119. See Carrier & Wander, *supra* note 5, at 275.

120. See *supra* Table 4.

28%, 4%, 7%, 5%, and 0%, with denial rates of 72%, 96%, 93%, 95%, and 100%.

Figure 2: Brand Win Rate by Year



V. 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. Petition Complexity

Citizen petitions are inherently complex and challenging because they allege that a pending generic does not meet pharmacokinetic and bioequivalence standards. 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.¹²¹ 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 down the FDA, which is forced to spend more resources reviewing lengthy petitions. In fact, congressional reports have repeatedly explained that complex petitions are draining the agency of time and resources better allocated to other functions.¹²²

Along those lines, it is concerning that, as seen in Table 5, the average length of a 505(q) petition has more than doubled from 2011 to 2015, from roughly 14 to 32 pages.¹²³ This trend is accelerating, increasing between 2011 and 2015 from 14 to 21, 21, 26, and 32 pages.

Table 5: Average Page Length of Citizen Petitions by Year

<i>Year</i>	<i>Average Page Length</i>
2011	14
2012	21
2013	21
2014	26
2015	32

While petitioners could conceivably claim that longer petitions reflect increased complexity and therefore more legitimate petitions that have a greater likelihood of success, the reality is 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 6, only 1 petition with a page length above the mean was granted in five years. Not including

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

122. See FY 2014 REPORT, *supra* note 95, at 7 (declaring that the FDA “redirect[ed] efforts” to comply with statutory time constraints for citizen petition responses, and implying that section 505(q) might contribute to better allocation of resources).

123. We ignored differences between single-spaced and double-spaced petitions, and also did not include appendices, which are less likely to receive careful attention, in the page count.

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 6: Results for Petitions Exceeding the Mean Page Length by Year

<i>Year</i>	<i>Granted</i>	<i>Denied</i>	<i>Other</i> ¹²⁴
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 a 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 long.¹²⁵ In 2012, when the average page length was 21, the only granted petition was 7 pages long.¹²⁶ In 2013, when the average page length was 21, the two granted petitions were 13 and 5 pages long.¹²⁷ And in 2014, when the average page length was 26, the only granted petition was 15 pages long.¹²⁸ In sum, long petitions seem geared not to

124. The “Other” category includes withdrawals and interim responses.

125. See Somaxon Pharmaceuticals Citizen Petition, No. FDA-2011-P-0767-0001 (Oct. 20, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0767-0001> (12 pages); Warner Chilcott Citizen Petition, No. FDA-2011-P-0575-0001 (Aug. 1, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0575-0001> (22 pages); Lehigh Valley Technologies, Inc. and Glenmark Generics, Inc. USA Citizen Petition, No. FDA-2011-P-0433-0003 (May 31, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0433-0003> (6 pages); Baxter Healthcare Citizen Petition, No. FDA-2011-P-0127-0001 (Mar. 1, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0127-0001> (5 pages); Pronova BioPharma Citizen Petition, No. FDA-2011-P-0120-0001 (Feb. 28, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0120-0001> (8 pages).

126. See Laboratorios SALVAT Citizen Petition, No. FDA-2012-P-0647-0001 (June 19, 2012), <https://www.regulations.gov/document?D=FDA-2012-P-0647-0001>.

127. See SUBOXONE Citizen Petition, No. FDA-2013-P-0995-0001 (Aug. 12, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-0995-0001> (13 pages); Watson Laboratories, Inc. Citizen Petition, No. FDA-2013-P-0664-0001 (June 4, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-0664-0001> (5 pages).

128. See Pfizer Inc. Citizen Petition, No. FDA-2014-P-1269-0001 (Aug. 18, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-1269-0001>. No petitions were granted in 2015.

raising legitimate safety concerns but to bogging down the FDA and delaying generic entry.

B. 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. We hypothesized that brands were filing petitions shortly before the expiration of a patent or data exclusivity. To test this hypothesis, we examined the 129 NDAs protected by the 124 petitions filed between 2011 and 2015.¹²⁹ In particular, we focused on exclusionary dates when these 129 NDAs would lose their "protected status" as a result of the approval of a pending generic.

We found that of the 129 protected NDAs, a petition was filed within a "late-filed" window of 6 months of an exclusionary date—either patent- or exclusivity-related—in 50 cases, or 39%. Of this 39%, 19% had a petition filed within 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 date and a data exclusivity date.¹³⁰ Table 7 presents our findings.

129. There are more NDAs implicated than number of petitions because a single petition can refer to more than one NDA. *See, e.g.*, Watson Laboratories, Inc. Citizen Petition, *supra* note 127, at 2 (implicating NDA 020756 and NDA 020701).

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

Table 7: *Petitions and Exclusionary Dates*¹³¹

	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 Date	2 (9%)	1 (3%)	2 (6%)	0 (0%)	0 (0%)	5 (4%)
Within 6 Months of an Exclusionary Date	6 (27%)	9 (30%)	17 (53%)	10 (40%)	8 (32%)	50 ¹³² (39%)

Of the 19% of petitions filed within 6 months of a patent expiration date, 16% of NDAs witnessed a petition filed within 6 months of the nearest expiration, while 3% had a petition filed within 6 months of the last expiration (“patent cliff”).

The prevalence of patents filed within 6 months of the nearest patent, rather than the patent cliff, makes sense. 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

131. 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 dates, we include that only in the penultimate row of the table.

132. 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 expiration to (2) the 32 petitions filed within 6 months of an exclusivity date, (3) subtracting the 5 petitions filed within 6 months of a patent expiration date *and* exclusivity date, and (4) subtracting the 2 petitions that were each filed within 6 months of two *separate* exclusionary dates. *See, e.g.*, Spectrum Pharmaceuticals, Inc. Citizen Petition, No. FDA-2014-P-1649-0001 (Sept. 30, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-1649-0001> (focusing on FUSILEV and representing a petition filed within 154 days of nearest exclusivity date and 178 days of final exclusivity date); Perrigo Co. Citizen Petition, No. FDA-2011-P-0840-0001 (Nov. 18, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0840-0001> (addressing Prevacid 24HR, NDA 020406, and representing a petition filed within 21 days of nearest exclusivity date and 162 days of final exclusivity date).

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 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 related to the process of how the drug can be formulated.¹³³ Because a brand firm 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.¹³⁴

These observations on the nature of drug patents are consistent with our findings. A petition challenging that approval process is more likely to occur closer to the expiration of nearest patents. 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 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. And

133. 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. See Otsuka Pharmaceutical Development & Commercialization, Inc. Citizen Petition, No. FDA-2014-P-1354-0001 (Sept. 10, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-1354-0001>. The last-to-expire patent for ABILIFY listed in the 2014 Orange Book, however, was slated to expire more than 3000 days later, on December 16, 2024. CTR. FOR DRUG EVALUATION & RESEARCH, FDA, APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, at ADA 16 (34th ed. 2014). The patent that will expire on December 16, 2024, U.S. Patent No. 8,017,615 (“the ‘615 Patent”), 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 because the ‘615 Patent claims a process. See MARTIN A. 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”).

134. See, e.g., Mylan Specialty, LP Citizen Petition, No. FDA-2015-P-0181-0001 (Jan. 16, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-0181-0001> (representing a petition aimed at Mylan's EpiPen, which had Orange Book-listed patents appear for the first time in 2009—more than *two decades* after EpiPen was first approved in 1987).

4% had a petition filed within 6 months of both a patent expiration date and a data exclusivity date.

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—witnessed 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 8, the FDA denied 49 of 50 petitions filed within 6 months of a protected NDA’s exclusionary date.¹³⁵ This paltry 2% grant rate further supports our hypothesis that late-filed petitions almost never raise valid safety concerns.

Table 8: 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

C. Same-Day Resolution of Petition and ANDA Approval

Another concerning aspect of petitions is the FDA’s resolution of them on the same day, or in the same month, that it approves the ANDA for the targeted generic product. 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.¹³⁶

135. For the sole grant, see SUBOXONE Citizen Petition, *supra* note 127 (containing a mixed, “essentially granted” decision, in which the FDA decided that an application seeking approval for generic SUBOXONE should include data proving minimal impurities).

136. The Second Circuit rejected a claim that a brand firm’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, 60 (2d Cir. 2016) (reasoning that the 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.

As we show in Table 9, the FDA approved 23 targeted ANDAs within one month after it resolved a 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 related petition in 2015. This reflects as many same-day resolutions as the previous 4 years combined.

Table 9: Same-Month Resolution of Petitions and ANDA Approval

<i>Year</i>	<i>Number of Petitions</i>	<i>ANDA Approved on Same Day</i>	<i>Additional ANDAs Approved within One Month</i>	<i>Petitions Granted</i>
2011	4	2	13 ¹³⁷	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 denial in court. The denial of a citizen petition is a final agency action under the Administrative Procedure Act, which means that an Article III court can review and reverse the agency's determination. Challenging

137. This number is high because on March 27, 2011, the FDA approved 10 separate generics referencing AstraZeneca Pharmaceuticals' SEROQUEL. This high number appears to be an outlier among the data.

the FDA's 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 because the generic has already penetrated the market, with the "damage" having already occurred. But another interpretation is that the FDA's resolution of the citizen petition within the same month—or especially on the same day—that it grants ANDA approval reveals 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 that the FDA resolved in the same month that it approved the ANDA were filed within 6 months of an exclusivity date.¹³⁸ As for the other two petitions, one dealt with Teva's multi-billion-dollar drug COPAXONE. As we discuss below,¹³⁹ Teva filed eight separate petitions asking the FDA to take actions on any ANDA referencing COPAXONE. The fifth petition was resolved four days before ANDA approval.¹⁴⁰ Again, as it did in *every case* in which the FDA resolved a petition within the same month it approved the generic, it denied the petition.

138. Teva Pharmaceuticals filed a petition within 36 days of an exclusivity date protecting TREANDA. *See* Teva Pharmaceutical Industries, Ltd. Citizen Petition, No. FDA-2015-P-3980-0001 (Oct. 26, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-3980-0001>. The FDA ultimately denied this petition on March 24, 2016—the same day that it approved two generics: ANDA 204771 and ANDA 205476. Because one petition targeted 2 generics, there are more ANDAs (6) than petitions (5) in 2015. 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. *See* Helsinn Healthcare SA Citizen Petition, No. FDA-2015-P-1722-0001 (May 13, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1722-0001>; Helsinn Healthcare SA Citizen Petition, No. FDA-2015-P-1721-0001 (May 13, 2015) [hereinafter Helsinn Citizen Petition 1], <https://www.regulations.gov/document?D=FDA-2015-P-1721-0001>. 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.

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

140. *See* Helsinn Citizen Petition 1, *supra* note 138.

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."¹⁴¹ Time will tell whether 2015 marks a trend of increasing simultaneous resolution.

VI. CASE STUDIES

The concerns mentioned above are not hypothetical. This Part introduces four case studies 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 became classics. In 2015, *Teva Pharmaceuticals USA v. Sandoz, Inc.*¹⁴² 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.¹⁴³ Underlying this important ruling is a story of Teva's robust life cycle management of COPAXONE—the \$3 billion per year multiple sclerosis drug.

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 2014.¹⁴⁴ Once generic firms filed for approval, Teva initiated patent litigation under the Hatch-Waxman Act.¹⁴⁵ But in addition to litigation, the company—in an action

141. 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/>.

142. 135 S. Ct. 831 (2015).

143. *Id.* at 836, 840.

144. Steven Ross Johnson, *First Generic for MS Drug Copaxone Launches in U.S.*, MOD. HEALTHCARE (June 19, 2015), <http://www.modernhealthcare.com/article/20150619/NEWS/150619886>; Gene Quinn, *Teva Sues Mylan over Multiple Sclerosis Drug Copaxone*, IPWATCHDOG (Oct. 18, 2009), <http://www.ipwatchdog.com/2009/10/18/teva-sues-mylan-over-multiple-sclerosis-drug-copaxone/id=6712>.

145. Quinn, *supra* note 144.

that has not received much attention—also filed *eight* separate citizen petitions with the FDA from 2008 through 2015.¹⁴⁶

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.¹⁴⁷ And in each of the eight petitions,¹⁴⁸ 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.¹⁴⁹ One aspect that Teva continually stressed was the lack of bioequivalence testing available for non-biological complex drugs.¹⁵⁰ The FDA nonetheless denied each of the eight petitions. The final denial came on the same day the FDA approved Sandoz's ANDA.¹⁵¹

146. *FDA Approves a Generic for Teva's Copaxone, Bringing Longstanding Regulatory Battles near an End*, PHARMACEUTICAL COM. (Apr. 16, 2015), <http://www.pharmaceuticalcommerce.com/latest-news/fda-approves-a-generic-for-tevas-copaxone-bringing-longstanding-regulatory-battles-near-an-end/>.

147. *See* Teva Neuroscience, Inc. Citizen Petition, No. FDA-2015-P-1050-0001 (Apr. 1, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1050-0001> (133 pages); Teva Neuroscience, Inc. Citizen Petition, No. FDA-2014-P-0933-0001 (July 2, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-0933-0001> (132 pages).

148. *See, e.g.*, Teva Neuroscience, Inc. Citizen Petition, No. FDA-2015-P-1050-0001 (Apr. 1, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1050-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2014-P-0933-0001 (July 2, 2014), <https://www.regulations.gov/document?D=FDA-2014-P-0933-0001>; Teva Pharmaceuticals Citizen Petition, No. FDA-2013-P-1641-0001 (Dec. 5, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1641-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2013-P-1128-0001 (Sept. 12, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1128-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2012-P-0555-0001 (June 4, 2012), <https://www.regulations.gov/document?D=FDA-2012-P-0555-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2010-P-0642-0001 (Dec. 10, 2010), <https://www.regulations.gov/document?D=FDA-2010-P-0642-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2009-P-0555-0001 (Nov. 13, 2009), <https://www.regulations.gov/document?D=FDA-2009-P-0555-0001>; Teva Neuroscience, Inc. Citizen Petition, No. FDA-2008-P-0529-0001 (Sept. 26, 2008), <https://www.regulations.gov/document?D=FDA-2008-P-0529-0001>.

149. Teva Neuroscience, Inc. Citizen Petition, No. FDA-2015-P-1050-0001, at 2–4 (Apr. 1, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1050-0001> (asserting that the complexity of COPAXONE includes unknown characteristics that are related to its safety and efficacy, so a generic could not contain the same active ingredient).

150. *See id.* (explaining that the scientific community does not yet know what type of tests or how much information is needed to determine bioequivalence for non-biological complex drugs like COPAXONE, and recognizing that all of the biologically active parts of a complex drug might need to be identified before establishing bioequivalence standards).

151. *Compare GLATOPA*, DRUGS @ FDA, <http://www.accessdata.fda.gov/scripts/>

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.¹⁵² Because biosimilars aim 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 that Teva filed in relation to COPAXONE.¹⁵³

B. MIRENA: Filing Immediately Before Patent Expiration

One example of the last-minute filings we discussed above¹⁵⁴ appears in the case of MIRENA, a long-acting 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 up to five years, twice as long as other IUD products.¹⁵⁵ MIRENA has carved out a market niche as a long-acting IUD.

On December 4, 2015, Bayer HealthCare filed a citizen petition with the FDA.¹⁵⁶ Of note, this petition was filed *one day before* the only patent protecting the drug was set to expire on December 5, 2015.¹⁵⁷

[cdcr/drugsatfda/index.cfm?fuseaction=Search.Set_Current_Drug&AppNo=090218&DrugName=GLATOPA&ActiveIngred=GLATIRAMER%20ACETATE&SponsorApplicant=SANDOZ%20INC&ProductMktStatus=1&goto=Search.DrugDetails](http://www.accessdata.fda.gov/drugsatfda/index.cfm?fuseaction=Search.Set_Current_Drug&AppNo=090218&DrugName=GLATOPA&ActiveIngred=GLATIRAMER%20ACETATE&SponsorApplicant=SANDOZ%20INC&ProductMktStatus=1&goto=Search.DrugDetails) (showing Sandoz-sponsored ANDA 090218, the only approved generic referencing COPAXONE, approved on April 16, 2015), *with* Teva Neuroscience, Inc. Citizen Petition, No. FDA-2015-P-1050-0001, at 2–4 (Apr. 1, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-1050-0001> (denied on April 16, 2015).

152. *See, e.g.*, PhRMA Citizen Petition, No. FDA-2015-P-5022-0001 (Dec. 22, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-5022-0001>.

153. 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 that use nanotechnology. Celgene Corp. Citizen Petition, No. FDA-2015-P-0732-0001 (Mar. 6, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-0732-0001>. 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 Celgene filed the petition.

154. *See supra* Section IV.C.

155. *Mirena*, DRUGS.COM, <https://www.drugs.com/pro/mirena.html> (last visited Nov. 30, 2016).

156. Bayer HealthCare LLC Citizen Petition, No. FDA-2015-P-4600-0001 (Dec. 4, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-4600-0001>.

157. *Compare id.*, *with* LEVONORGESTREL (MIRENA) INTRAUTERINE DEVICE 52MG, *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, FDA, http://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=

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 November 2016, almost one year had passed since Bayer filed the petition without a clear grant or denial from the FDA. This is more than *double* the time mandated pursuant to the FDAAA 150-day response period.¹⁵⁸ Given that there is little public information on generics in the pipeline, the strategy behind the filing of the MIRENA petition is not clear. But at a minimum, the fact that the petition was filed *one day* before expiration of the only patent protecting the drug strongly suggests that the company was interested in extending its exclusivity and ensuring that generics would be blocked from entering the market.¹⁵⁹

C. DORYX: Combination of Citizen Petitions and Product Hopping

Another concerning example is the use of citizen petitions together 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 Chilcott¹⁶⁰ engaged in a decade-long effort to avoid direct competition with generic powerhouse, Mylan.¹⁶¹ The product at issue, DORYX, is used to treat acne. An immediate-release capsule version of the drug has been available since the 1960s.¹⁶²

001&Appl_No=021225&Appl_type=N (listing U.S. Patent No. 5,785,053 and expiration date of Dec. 5, 2015) (last visited Nov. 30, 2016).

158. 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 mechanisms by which this timeframe can be enforced. The FDA's failure to meet the 150-day period undermines Congress's intent.

159. The suspicious timing of Bayer's petition regarding MIRENA is not unique. For a few other examples, see Cadence Pharmaceuticals, Inc. Citizen Petition, No. FDA-2013-P-1508-0001 (Nov. 4, 2013), <https://www.regulations.gov/document?D=FDA-2013-P-1508-0001>. (OFIRMEV, petition filed within 2 days of data exclusivity expiration); Sunovion Pharmaceuticals, Inc. Citizen Petition, No. FDA-2012-P-0943-0001 (Aug. 29, 2012), <https://www.regulations.gov/document?D=FDA-2012-P-0943-0001> (LUNESTA, petition filed within 1 day of nearest Orange Book-listed patent expiration); AstraZeneca Pharmaceuticals LP Citizen Petition, No. FDA-2011-P-0823-0001 (Nov. 14, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0823-0001> (CRESTOR, petition filed within 8 days of nearest data exclusivity expiration).

160. Warner Chilcott marketed DORYX in the United States along with Mayne Pharmaceuticals. We refer solely to Warner Chilcott, which has been acquired by Actavis.

161. For a complete recitation of the facts regarding the DORYX product hopping case, see *Mylan Pharmaceuticals, Inc. v. Warner Chilcott Pub. Co.*, No. 12-3824, 2015 WL 1736957, at *1-5 (E.D. Pa. Apr. 16, 2015), *aff'd*, No. 15-2236, 2016 WL 5403626 (3d Cir. Sept. 28, 2016).

162. *Mylan Pharm.*, 2015 WL 1736957, at *2.

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 unscored¹⁶³ tablets.¹⁶⁴ One year later, Mylan began developing generic 75-mg and 100-mg unscored tablets.¹⁶⁵ Over the next seven years, Warner obtained various FDA approvals for tablets ranging from 75 mg to 150 mg, including such doses in single- and dual-scored tablet form.¹⁶⁶ 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.¹⁶⁷

In January 2009, Warner Chilcott began to aggressively market a 150-mg, single-scored DORYX tablet.¹⁶⁸ Within a few months, this version of the tablet represented 71% of new DORYX prescriptions.¹⁶⁹ One year later, 90% of patients had been switched to this version.¹⁷⁰ In the meantime, beginning in March 2010, Warner Chilcott began to develop a 150-mg, *dual*-scored version of the tablet.¹⁷¹ In June 2011, the FDA granted tentative approval for Mylan's generic 150-mg, single-scored version.¹⁷² Mylan had filed this ANDA almost three years earlier, in December 2008.¹⁷³ 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.¹⁷⁴

163. "Unscored" means that there is no notch in the tablet to make it easier for a patient to split the tablet. CTR. FOR DRUG EVALUATION & RESEARCH, FDA, TABLET SCORING: NOMENCLATURE, LABELING, AND DATA FOR EVALUATION 1 n.2 (2013) (defining a score as "a debossed line that runs across the planar surface of the tablet" to facilitate tablet splitting). For example, if a patient is prescribed two daily doses of 50 mg, then the patient can split a single-scored 100-mg tablet.

164. *Mylan Pharm.*, 2016 WL 5403626, at *3.

165. *See id.* at *4.

166. *Id.* at *3–4.

167. 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. *See Mylan Pharm.*, 2015 WL 1736957, at *3. 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 the generic entered.

168. *See Mylan Pharm.*, 2015 WL 1736957, at *3.

169. *Id.*

170. *Id.*

171. *Id.*

172. *See id.* at *4.

173. *Id.*

174. *See Mylan Pharm., Inc. v. Warner Chilcott Pub. Co.*, No. 15-2236, 2016 WL 5403626 (3d Cir. Sept. 28, 2016), at *4.

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.¹⁷⁵ 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.¹⁷⁶ Warner Chilcott argued that patients would be confused if both single- and dual-scored 150 mg tablets were available.¹⁷⁷

The FDA denied this petition 138 days later on February 8, 2012.¹⁷⁸ On that *same day*, the FDA gave final approval to Mylan’s ANDA for a 150-mg, single-scored tablet and granted it an AB-rating for Warner Chilcott’s dual-scored version.¹⁷⁹ Mylan launched its generic 150-mg, single-scored version immediately thereafter.¹⁸⁰ 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 for more than four months.

175. Warner Chilcott, LLC Citizen Petition, No. FDA-2011-P-0702-0001 (Sept. 23, 2011), <https://www.regulations.gov/document?D=FDA-2011-P-0702-0001>.

176. *Id.* at 1.

177. *Id.* at 5 n.24.

178. Letter from Janet Woodcock, M.D., Dir., Ctr. for Drug Evaluation and Research, to Izumi Hara, Senior Vice President & Gen. Counsel, Warner Chilcott (US), LLC (Feb. 8, 2012), <https://www.pharmamedtechbi.com/~media/supporting%20documents/The%20Pink%20Sheet/FDA%20letter%20denying%20Warner%20Chilcotts%20citizen%20petition.pdf>.

179. *Mylan Receives Final FDA Approval for First Generic Version of Doryx Tablets, 150 mg*, FIERCEPHARMA (Feb. 9, 2012, 8:20 AM) [hereinafter *Mylan Final Approval*], <http://www.fiercepharma.com/pharma/mylan-receives-final-fda-approval-for-first-generic-version-of-doryx%C2%AE-tablets-150-mg>; see Carrier, *supra* note 33, at 1018 (indicating that an AB rating allows pharmacists to substitute generic versions of brand drugs).

180. *Mylan Final Approval*, *supra* note 179.

D. EpiPen: Citizen Petitions, Settlements, and Price Hikes

Mylan's billion-dollar EpiPen presents the final example of dubious uses of citizen petitions.¹⁸¹ Initially approved in 1987, EpiPen auto-injectors are the primary means of treating severe allergic reactions.¹⁸² Mylan received significant unwanted attention in 2016 for its price hike of the EpiPen,¹⁸³ but its citizen petition largely escaped notice. The lifecycle of the 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. Mylan commenced litigation against Teva,¹⁸⁴ and the parties settled in April 2012.¹⁸⁵ Under the terms of the settlement, Teva agreed to delay the launch of its generic epinephrine auto-injector for more than three years, until June 2015.¹⁸⁶

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.¹⁸⁷ In its petition, Mylan contended that Teva should be required to demonstrate that its product was the "same as"

181. *Mylan Sales and Revenue up While EpiPen Becomes Its First \$1 Billion-Selling Product*, PHARMA LETTER (Mar. 3, 2015), <http://www.thepharmaletter.com/article/mylan-sales-and-revenue-up-while-epipen-becomes-its-first-1-billion-selling-product>.

182. *EpiPen*, DRUGS.COM, <https://www.drugs.com/pro/epipen.html> (last visited Nov. 30, 2016).

183. See, e.g., Olga Khazan, *Have You Ever Tried to Buy an EpiPen?*, ATLANTIC (Aug. 24, 2016), <http://www.theatlantic.com/health/archive/2016/08/epi-pens/497126/>; Andrew Pollack, *Mylan Raised EpiPen's Price Before the Expected Arrival of a Generic*, N.Y. TIMES (Aug. 24, 2016), http://www.nytimes.com/2016/08/25/business/mylan-raised-epipens-price-before-the-expected-arrival-of-a-generic.html?_r=0.

184. Complaint, *King Pharm., Inc. v. Teva Parenteral Meds., Inc.*, (D. Del. Aug. 28, 2009) (No. 09-CV-00652).

185. See Pollack, *supra* note 183.

186. See Press Release, Mylan, Mylan and Pfizer Announce Epinephrine Auto-Injector Settlement Agreement with Teva (Apr. 26, 2012), <http://newsroom.mylan.com/press-releases?item=123144>; see also 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-> (suggesting that Teva might experience a longer-than-expected delay because it would need the FDA to approve its generic before it could enter the epinephrine-pen market).

187. Mylan Specialty LP Citizen Petition, No. FDA-2015-P-0181-0001 (Jan. 16, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-0181-0001>. Mylan may have known about Teva's ANDA as early as 2008. See Michael A. Carrier & Carl J. Minniti, *The Untold EpiPen Story: How Mylan Hiked Prices by Blocking Rivals*, 102 CORNELL L. REV. ONLINE (forthcoming 2016) (manuscript at 10), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2841445.

Mylan's EpiPen.¹⁸⁸ 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 correctly.¹⁸⁹

Given that Teva's generic had been in development for at least *six years* before the petition's filing,¹⁹⁰ 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?¹⁹¹

Even though Teva's ANDA ultimately was denied in the spring of 2016,¹⁹² the petition still raises concern since Mylan (1) could not have known at the time of filing that the FDA would deny the application and (2) increased the likelihood of delay through its stalled petition and supplemental filing.

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 incidence of the FDA

188. *Id.*

189. Supplement from Mylan Generic Epinephrine Auto-Injector Handling Study, No. FDA-2015-P-0181-0008, at 45 (May 28, 2015), <https://www.regulations.gov/document?D=FDA-2015-P-0181-0008>.

190. See Carrier & Minniti, *supra* note 187, at 9–10.

191. The study also apparently “had a lot of problems” as it “lacked a control group; did not study the actual generic but a prototype instead; used a small number of participants; failed to provide them with proper instructions for use; and told participants to watch a video rather than actually use the Teva device.” Ed Silverman, *How Mylan Tried to Keep Teva from Selling a Generic EpiPen*, STAT (Aug. 31, 2016), <https://www.statnews.com/pharmalot/2016/08/31/mylan-teva-generic-epipen/>.

192. Carly Helfand, *FDA Swats down Teva's EpiPen Copy, Putting Mylan in Cruise Control*, FIERCEPHARMA (Mar. 1, 2016, 10:39 AM), <http://www.fiercepharma.com/sales-and-marketing/fda-swats-down-teva-s-epipen-copy-putting-mylan-cruise-control>.

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.