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A Citizen's Pathway Gone Astray — Delaying Competition from Generic Drugs

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The compromises under discussion between the White House and House Republicans — enabling states to opt out of ACA provisions requiring that insurers not charge sicker persons higher premiums (community rating) and provide essential health benefits (such as maternity services) — could further alienate moderate Republicans who are already uncomfortable with the bill's effect on Medicaid and insurance coverage. The changes the House bill makes to insurance regulation also could run afoul of Senate budget reconciliation rules. And rolling

 An audio interview with Dr. Oberlander is available at NEJM.org

back the ACA's popular consumer protections, including those for persons with preexisting conditions, will spark additional controversy. Thus, the prospects of GOP efforts to resurrect repeal and replace remain highly uncertain.

If Republicans cannot pass re-

peal legislation, the Trump administration has other options to undermine Obamacare, including weakening enforcement of penalties for not obtaining insurance and eliminating federal payments to insurers that are required to provide cost-sharing subsidies to lower-income Americans for deductibles and copayments.⁵ Such actions could explode the individual insurance marketplaces. The ACA's insurance exchanges remain vulnerable: in some states they have been buffeted by high premium increases and insurer withdrawals. The continuing uncertainty over the ACA's fate could lead more insurers to exit these marketplaces, potentially leaving Americans in some areas of the country with no options for buying subsidized coverage.

President Trump remarked that “nobody knew that health care could be so complicated.” Republicans' struggles to turn their

repeal-and-replace rhetoric into reality underscore just how complicated it is.

Disclosure forms provided by the author are available at NEJM.org.

From the University of North Carolina, Chapel Hill.

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A Citizen's Pathway Gone Astray — Delaying Competition from Generic Drugs

Robin Feldman, J.D., and Connie Wang, B.A.

Many medicines are making headlines these days not for their breathtaking ability to save lives, but for their soaring prices. Part of the problem occurs because pharmaceutical companies have become adept at converting regulatory pathways into vehicles for profit-boosting pricing strategies. Consider the citizen-petition process that the Food and Drug Administration (FDA) implemented in the 1970s to give the average citizen a way to voice concerns. A recent large-scale study we con-

ducted using 12 years of FDA data reveals that the concerned citizen is frequently a drug company raising frivolous or questionable claims in a last-ditch effort to hold off competition.^{1,2}

The Hatch–Waxman Act of 1984 created a regulatory regime to facilitate rapid market entry of generics, allowing manufacturers of generic drugs to rely on clinical trial data from their drugs' brand-name counterparts. Today, more than three quarters of prescriptions are filled with generic

versions, whose availability can reduce the price of a drug substantially. In response, drug companies have developed complex strategies to block entry by generics. Their incentive is clear: delaying competition for just a few months can translate into hundreds of millions of dollars in revenue.

Focusing on strategies that involve manipulation of the citizen-petition pathway, we analyzed the timing of the filing of citizen petitions relative to the filing and

approval of the generics that they had the potential to block. We hypothesized that filings would be concentrated toward the end of the generic drug's approval process, acting as a final barrier to market entry.

In examining all citizen petitions filed between 2000 and 2012 that could have delayed a generic's market entry, we found widespread, strategic use of the citizen-petition pathway by drug companies striving to hold off competition. Specifically, nearly half of the petitions in the final data set were filed within a year and a half before the FDA approved the generic, with roughly 40% filed a year or less before generic approval (see graph). The clustering of filings at the end of the approval process suggests that the motive is delay. It is possible that the company filing the petition became aware of the problem it purported to see with its competitor's application only late in the process. The FDA has noted, however, that many petitions "contained data that had been available to the petitioner well before the date of the petition."³ Thus, it

appears that a large proportion of drug companies are using citizen petitions as an 11th-hour effort to prevent generic competitors from gaining FDA approval and entering the market.

Use of this delay strategy has increased over the past decade: the number of such petitions filed has effectively doubled since 2003 (see table). In some years, one of every five FDA citizen petitions (which include petitions related to devices, food, dietary supplements, and tobacco, as well as to drugs) has had the potential to obstruct generic competition.

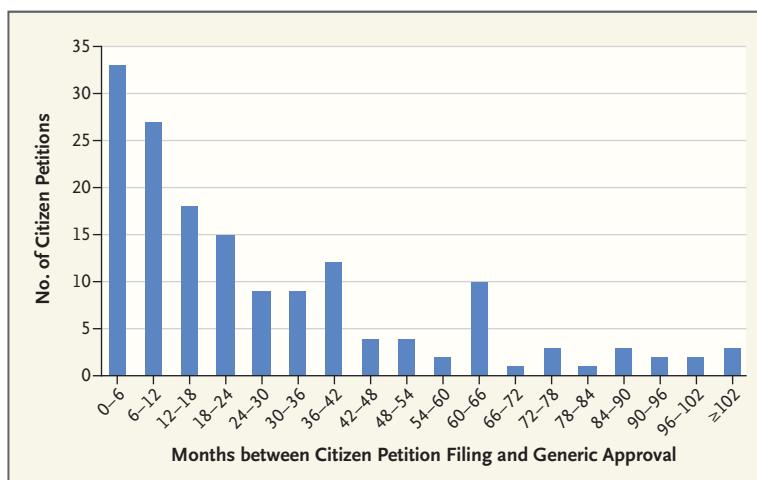
Some petitions we examined did appear to raise legitimate concerns, and the FDA ruled accordingly. For example, in 2003, Wyeth Pharmaceuticals asked the FDA to refrain from approving generic versions of its immunosuppressant Rapamune (sirolimus), whose makers had removed part of the labeling. The FDA agreed that omitting the labeling, which described a regimen to reduce the risk of renal function impairment, created safety concerns.

Such petitions, however, appear to be the exception rather than

the rule. The FDA denies the requested action for approximately 80% of citizen petitions filed by competitors against drug companies.⁴ For example, in 2007, Mutual Pharmaceuticals asked the FDA to delay approval of other generic versions of the blood-pressure medicine Plendil (felodipine), citing concerns about how Seville orange juice, as opposed to "regular" orange juice, affected absorption. Seville oranges are a smaller, more bitter orange often used for marmalade and liquors. The FDA denied the petition, stating that Mutual had "offered no data to support [its] hypothesis." Another illustrative case is the petition filed by Warner Chilcott regarding its acne medication Doryx (doxycycline). On the eve of generic approval, Warner began marketing Doryx tablets with two score lines as opposed to one and asked the FDA to require that all generic versions also be dual-scored. Citing the lack of any safety concern associated with single-scored tablets, the FDA denied the petition and immediately approved a single-scored generic.

Yet some petitions representing pure delay tactics have been granted. For instance, many petitions ask the FDA to stay approval of the generic version until the applicant conducts a test that is already required for approval. The FDA is forced to grant the petition, even though the demands are redundant given the existing requirements.

In 2007, Congress amended the FDA Act in an attempt to block potential avenues for abuse, requiring that the agency respond to citizen petitions related to generics within 180 days (shortened to 150 days in 2012) and providing that the agency can summarily deny petitions that are intend-



Months between Citizen Petition Filing and Generic Approval, 2000–2012.

Ranges of months along the x axis indicate the period from the lower number up to but not including the higher number. Data are from Feldman et al.¹

Delay-Related Citizen Petitions, by Year.*		
Year	No. of Delay-Related Petitions	Percent of All Petitions (no./total no.)
2000	2	4.3 (2/47)
2001	4	6.3 (4/63)
2002	5	4.7 (5/106)
2003	12	10.0 (12/120)
2004	26	14.6 (26/178)
2005	15	10.1 (15/148)
2006	24	13.0 (24/184)
2007	25	15.6 (25/160)
2008	23	13.9 (23/166)
2009	32	18.7 (32/171)
2010	31	20.8 (31/149)
2011	22	14.0 (22/157)
2012	28	19.9 (28/141)

* Data are from Feldman et al.¹

ed to delay generic entry and “raise no valid scientific or regulatory issues.” Unfortunately, the 2007 amendments have been largely toothless. Imposing a new deadline may have reduced the delay between when the FDA would have approved the generic and when it actually did so after reviewing the petition, but our data show that the number of delay-related petitions continued to grow after the amendments were passed. Moreover, as of fiscal year 2014, the FDA had not summarily denied a single petition under the relevant provision.⁵

What policies may succeed where the 2007 amendments have floundered? One option is to simply prohibit companies from filing citizen petitions referencing generic-drug applications. Companies could continue to submit generalized petitions, however, such as those asking the FDA to reconsider all labeling related to a given drug. Such petitions would have the effect of delaying mar-

ket entry of generics without explicitly naming them. Moreover, some company petitions are justified, and safety must remain the FDA’s priority.

Another possible remedy would be to pursue punitive measures to deter pharmaceutical companies from manipulating the citizen-petition process. For example, on February 7, 2017, the Federal Trade Commission filed an antitrust action against Shire ViroPharma, alleging that the company abused regulatory processes by filing 43 submissions with the FDA (including 24 meritless citizen-petition filings within one docket) in an effort to hold off generic competition for its gastrointestinal drug Vancocin (vancomycin). According to the complaint, the behavior resulted in costs to patients and other purchasers amounting to hundreds of millions of dollars. Antitrust actions are expensive, however, and the burdens of proof under current law make it difficult for the government to pursue such actions.

We believe the most promising approach would be to erect procedural blocks, and in November 2016, new FDA rules took small steps toward doing so. For example, the new rules specify that the FDA cannot delay approval of a pending generic drug unless “a delay is necessary to protect the public health.” In general, however, the rules follow the same format as before, in which the definition of delay of approval, the timing of the process, and the limited remedies available leave plenty of room for strategic behavior. Stronger procedural blocks — such as requiring that drug companies file their citizen petitions within a year after the generic company files its application, or establishing that

issues raised by petitions will be resolved on a separate timeline from the generic’s approval process — are needed to reduce incentives for strategic efforts to undermine competition.

Regardless of the policy approach taken, greater transparency is essential. As we collected data, gaps in the FDA’s current system for publicly available information came into sharp relief. Finding information as basic as application filing dates for generic drugs required poring through volumes of letters and approval documents, and the information we sought was often entirely absent. Without increased transparency, society cannot curb strategic behaviors such as citizen-petition abuse. And as always, the public pays the cost.

Disclosure forms provided by the authors are available at NEJM.org.

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