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## Improving Generic Drug Approval at the FDA

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# IMPROVING GENERIC DRUG APPROVAL AT THE FDA

*Kathleen Craddock\**

*Generic drugs are the store-brand cereal of the drug world. While they lack the vibrant colors of and exciting commercials behind name brands, generics are still effective. Most importantly, for some people, they make the difference between accessing essential treatment and going without. Getting generics to market as quickly as possible means fewer people will cut pills in half or skip doses to save money, which also saves billions of dollars across the U.S. health system.<sup>1</sup> Because a new generic does not offer lifesaving changes for people with rare or complicated diseases, generics lack the “cultural capture of rhetoric about saving lives by getting new drugs to patients more quickly.”<sup>2</sup>*

*But generics are the drugs that many of us take every day. Generic drugs’ ease of entry into the market impacts whether everyday Americans can afford health insurance and access healthcare.*

*Better recognition of these benefits combined with insurer buy-in to the Food and Drug Administration’s (“FDA”) generic approval program has the potential to improve health while reducing systemic costs. This Note proposes three changes to the current approval process for generic drugs at FDA. First, the FDA should conduct a regular study to identify drugs that feature the biggest negative medication adherence impact.<sup>3</sup> Second, the FDA should allow insurers to sponsor generic approval for those drugs. Third, the FDA should be required to engage healthcare stakeholders beyond generic drug makers and manufacturers when it negotiates generic drug approval funding with industry.*

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\* Kathleen Craddock is a 2018 Juris Doctor candidate at the University of Michigan Law School and a Notes Editor for the *Michigan Journal of Environmental & Administrative Law*. She thanks the MJEAL editors for their support and assistance on this Note.

1. See Margaret A. Hamburg M.D., Comm’r of Food & Drugs, Food & Drug Admin., Remarks as Delivered at the GPhA Annual Meeting 3 (Feb. 22, 2013).

2. Donald W. Light et al., *Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs*, 14 J. OF L. MED. & ETHICS 590, 595 (2013).

3. Medication adherence measures whether patients take medication as prescribed by their medical providers without skipping or reducing doses. See, e.g., 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, 295 n.6 (2015).

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INTRODUCTION

Scientific breakthroughs that make deadly diseases treatable are understandably exciting and newsworthy. However, preventing runaway health costs and improving medication access may be more valuable to under-resourced communities and to the country overall. The Affordable Care Act was premised on this idea that we can afford to extend health care to more people if we can slow the growth of healthcare costs.<sup>4</sup> One way to slow healthcare cost growth is to embrace generics drugs. These drugs are sold at much lower prices than branded drugs for a number of reasons including their lack of patent protection.<sup>5</sup>

The FDA is charged with reviewing prescription drugs for safety and effectiveness.<sup>6</sup> FDA’s drug review is housed in the Center for Drug Evaluation and Research, which “perform[s] an essential public health task by making sure that safe and effective drugs are available to improve the health of people in the United States.”<sup>7</sup> FDA’s budget is supported by a mix of Congressional appropriations and user fees.<sup>8</sup> The FDA has four separate “user

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4. *Better Care, Smarter Spending, Healthier People: Improving Our Health Care Delivery System*, CTR. FOR MEDICARE & MEDICAID SERV., <https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-01-26.html> (Jan. 26, 2015).

5. *Generic Drugs: Questions and Answers*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm#q4> (last visited Mar. 8, 2018).

6. *About FDA: What We Do*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/AboutFDA/WhatWeDo/> (last visited Mar. 8, 2018).

7. *About the Center for Drug Evaluation and Research*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm> (last visited Mar. 8, 2018).

8. See Margaret Gilhooley, *Drug User Fee Reform: The Problem of Capture and a Sunset, and the Relevance of Priorities and the Deficit*, 41 N.M. L. REV. 327 *passim* (2011) (arguing the balance of FDA funding should shift more towards appropriations and away from user fees).

fee” programs where industry applicants for FDA approval pay FDA fees for processing applications: branded drugs (the Prescription Drug User Fee Act (“PDUFA”)), medical devices, generic drugs (the Generic Drug User Fee Act (“GDUFA”)), and biosimilar drugs.<sup>9</sup> This Note will focus on branded and generic drugs. Branded drugs are those drugs with patent and regulatory protection that often appear in commercials, such as Prilosec and Claritin.<sup>10</sup> Conversely, generic drugs are the un-branded versions that appear after the branded drugs have lost patent and regulatory protection, like omeprazole and loratadine.<sup>11</sup>

The user fee programs are reauthorized every five years in a comprehensive FDA reauthorization package.<sup>12</sup> The legislative language is accompanied by additional detail in documents called “Commitment Letters,” negotiated between the FDA and each relevant industry.<sup>13</sup> The Commitment Letters go beyond the broad legislative language, such as specifying the communication protocols between the FDA and industry while a drug application is pending.<sup>14</sup> Generic drugs are a new addition to this structure.<sup>15</sup> The generic user fee program started in 2012 and was recently reauthorized for the first time as part of the FDA Reauthorization Act of 2017.<sup>16</sup>

Generics provide savings for consumers in both co-pays and out-of-pocket costs, as well as for third-party payers.<sup>17</sup> In today’s world of high health insurance deductibles and co-pays, cost has a growing impact on

9. Zachary Brennan, *Regulatory Explainer: FDA User Fee Reauthorizations from 2018 to 2022*, REG. AFF. PROF. SOC’Y (Aug. 21, 2017), <http://www.raps.org/Regulatory-Focus/News/2017/08/21/28282/Regulatory-Explainer-FDA-User-Fee-Reauthorizations-From-2018-to-2022/>.

10. See FOOD & DRUG ADMIN., ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (2017), <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm> [hereinafter ORANGE BOOK].

11. Omeprazole is the generic version of Prilosec, and loratadine is the generic version of Claritin. See ORANGE BOOK, *supra* note 10.

12. Food & Drug. Admin. Reauthorization Act of 2017, 21 U.S.C. §§ 292-393 (2012).

13. See Brennan, *supra* note 9.

14. See FOOD & DRUG ADMIN., GDUFA II COMMITMENT LETTER: GDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROGRAM ENHANCEMENTS FISCAL YEARS 2018-2022, at 20 (2016) [hereinafter GDUFA II LETTER]; FOOD & DRUG ADMIN., PDUFA COMMITMENT LETTER: REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022, <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf> [hereinafter PDUFA LETTER].

15. Patrick O’Leary, *Funding the FDA: Assessing the User Fee Provisions of the FDA Safety and Innovation Act of 2012*, 50 HARV. J. ON LEGIS. 239, 247 (2013).

16. Brennan, *supra* note 9.

17. *Id.*

whether patients take the drugs their doctors prescribe.<sup>18</sup> Currently, retail prices for generic drugs for Medicare Part D patients are seventy-five to ninety percent lower than their brand-name counterparts.<sup>19</sup> High drug costs can cause elderly patients to take less than their prescribed medication dose or to not fill their prescriptions at all.<sup>20</sup> Since Medicare is not permitted to negotiate prices, market pressure brought about by cheaper generic alternatives to brand drugs may be the best way to ensure drug prices are affordable for seniors.<sup>21</sup>

The FDA has made significant strides to improve generic drug approval, but the generic drug industry would benefit from having public health advocates in its corner. Branded drug companies can afford to advocate for themselves in front of the FDA, but the generic drug industry runs on much tighter budgets.<sup>22</sup> The industry also requires additional sources of funds to pay the FDA's user fees to ensure the stability of generic drug approval going forward. This progress can be protected and furthered by three modifications to the current generic user fee program: identifying particular public health needs, sourcing additional funds for user fees, and engaging a broader healthcare stakeholder community.

First, the FDA should conduct a biennial series of studies of medication adherence, health outcomes, and overall cost of care based on generic availability for specific drugs widely used by vulnerable patient populations with

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18. Kesselheim & Darrow, *supra* note 3, at 317 (citing Thomas S. Rector & Patricia J. Venus, *Do Drug Benefits Help Medicare Beneficiaries Afford Prescribed Drugs?*, 23 HEALTH AFF. 213, 219 (2004)) (survey of 1,500 elderly Medicare beneficiaries with chronic health conditions, finding 32% opted not to fill prescription or take prescribed medication dose due to high out-of-pocket costs).

19. U.S. GOV'T ACCOUNTABILITY OFF., GAO-16-706, *GENERIC DRUGS UNDER MEDICARE: PART D GENERIC DRUG PRICES DECLINED OVERALL, BUT SOME HAD EXTRAORDINARY PRICE INCREASES* 1 (2016).

20. Kesselheim & Darrow, *supra* note 3, at 317 (citing Rector & Venus, *supra* note 18, at 219).

21. LARS NOAH, LAW, MEDICINE, AND MEDICAL TECHNOLOGY: CASES AND MATERIALS 866 (3d ed. 2012) (explaining that the Medicare Modernization Act of 2003 included a provision prohibiting the federal government from negotiating with drug makers when the Act created Part D Medicare coverage for prescription drugs).

22. Neeraj Sood et. al, *Follow the Money: The Flow of Funds in the Pharmaceutical Distribution System*, HEALTH AFF. (June 13, 2017), <https://www.healthaffairs.org/doi/10.1377/hblog20170613.060557/full/>. This Note does not analyze the possible implications of alleged antitrust violations in the form of price fixing in the generic industry or what is otherwise known about generic industry structure and profitability. For more on this developing issue, see Charles Lane, *Probe Into Generic Drug Price Fixing Set To Widen*, NPR (Mar. 7, 2018), <https://www.npr.org/2018/03/07/590217561/probe-into-generic-drug-price-fixing-set-to-widen>; see also Robert Freeman, *Allegations of Generic Drug Price Fixing Are Troubling*, THE HILL (Mar. 13, 2018), <http://thehill.com/opinion/healthcare/378165-allegations-of-drug-price-fixing-are-troubling>.

chronic conditions to identify drugs most in need of generic competition. Second, Congress should amend Title III of the FDA Reauthorization Act of 2017 (GDUFA II) to allow insurers to sponsor generic entry for drugs that improve health outcomes for vulnerable populations. This additional funding would provide needed support to help generics target the branded drugs where competition is most critical. Finally, the FDA should build on its recent efforts by committing to regularly engaging public health advocates in reauthorizing the FDA's generic drug approval program.<sup>23</sup>

This Note first provides an overview of the FDA drug approval process and the introduction of user fees from drug makers as a major source of the FDA's funding. This Note then discusses the successes of user fee funding in speeding branded drug approvals at the FDA and the approval backlog that has dogged generics. Next, this Note provides a set of three proposals to improve generic drug approval. Finally, this Note describes how user fees from generic drug makers have not fixed approval backlogs as rapidly as user fees from branded drug makers did and compares the most recent reauthorizations and stakeholder communities for branded drug fee funding and generic drug fee funding, demonstrating the need for the proposed improvements.

## I. BACKGROUND ON GENERIC DRUG APPROVAL

Prior to 1984, generic drugs struggled to obtain FDA approval because of the prohibitive costs generics incurred to prove that their drugs were safe.<sup>24</sup> Only nineteen percent of FDA-approved drugs were generics.<sup>25</sup> Showing safety and efficacy through clinical trials was too costly when a firm did not stand to earn the typically high profits available to the first branded drug on the market, referred to as "pioneer drugs."<sup>26</sup>

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act (commonly referred to as "Hatch-Waxman").<sup>27</sup> This law allows generic drug makers to piggyback on the pioneer drug's clinical trials

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23. See Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access, Request for Comments, 82 Fed. Reg. 28,493 (June 22, 2017) (seeking input from interested stakeholders on regulatory and legal obstacles to vigorous generic drug competition).

24. Rebecca Eisenberg & John R. Thomas, *Patents and Regulatory Exclusivity in the U.S.*, in FOOD & DRUG ADMIN. LAW COURSEPACK, 6 (Univ. Mich. Law Sch. 2014).

25. U.S. GOV'T ACCOUNTABILITY OFF., GAO-12-371R, DRUG PRICING: RESEARCH ON SAVINGS FROM GENERIC DRUG USE 2 (2012).

26. Eisenberg & Thomas, *supra* note 24, at 6.

27. SUSAN THAUL & JUDITH A. JOHNSON, CONG. RESEARCH SERV., R42540, PROPOSED FDA USER FEE ACTS: GENERIC DRUG USER FEE AMENDMENTS OF 2012 AND BIOSIMILAR USER FEE ACT OF 2012, at 5 (2012).

establishing safety and efficacy.<sup>28</sup> Under Hatch-Waxman, a generic drug maker may use an abbreviated new drug application (“ANDA”), instead of the more complicated new drug application (“NDA”). The ANDA process allows generic drug makers to get FDA approval when the drug maker proves their formulation is bioequivalent to the branded drug and will have the same use conditions, active ingredients, administration route, strength, and labeling as its branded counterpart.<sup>29</sup> Proving bioequivalence is much simpler and less costly than proving safety and efficacy for a new drug, providing particular savings in reduced need for extended clinical trials.<sup>30</sup>

Branded drugs can charge high prices while under patent or “regulatory exclusivity” protection, laws which protect their status as the only FDA-approved producer of a particular drug.<sup>31</sup> Patents on most inventions expire after twenty years, but branded drugs lose some of that time while the drug goes through clinical trials and regulatory review.<sup>32</sup> Hatch-Waxman provides branded drugs with patent term extensions of up to five years to recoup the lost time, capping the extension at fourteen years of patent protection after FDA approval.<sup>33</sup> Regulatory exclusivities that bar generic entry may apply as well, such as seven years of market exclusivity for “orphan” drugs treating a condition impacting fewer than 200,000 people in the U.S. and six months of market exclusivity for branded drugs that complete clinical trials to certify the drug for use in pediatrics.<sup>34</sup>

While generic drugs would not earn high profits from patent-based exclusivity, the law created a non-patent exclusivity period specifically for generics. Under Hatch-Waxman, the first generic firm to successfully challenge the branded drug’s patent protection under a certification that it is “invalid or will not be infringed” has 180 days to exclusively market its generic before the FDA will approve another generic competitor for that product.<sup>35</sup> Hatch-Waxman created this incentive to compensate generics for the expense of patent litigation against branded drug firms sparked by the noninfringement certification and to encourage generic entry as soon as patent and regulatory exclusivities allow.<sup>36</sup> By 2013, nearly eighty-five percent of all prescriptions filled in the U.S. were generic, and generic drugs

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28. *Id.*

29. Eisenberg & Thomas, *supra* note 24, at 7 (citing 21 U.S.C. § 355(j)(2)).

30. See Kesselheim & Darrow, *supra* note 3, at 302.

31. Eisenberg & Thomas, *supra* note 24, at 12-19.

32. *Id.* at 5.

33. *Id.* at 5-6.

34. *Id.* at 13, 18.

35. *Id.* at 7 (citing 21 U.S.C. § 355(j)(2)(A)(7)(vii)(IV)).

36. Kesselheim & Darrow, *supra* note 3, at 326.

saved consumers approximately \$1 trillion dollars in health care costs.<sup>37</sup> This was due to generics' low retail price, which is on average "about 25% of their brand-name counterparts."<sup>38</sup>

## II. INTRODUCTION OF THE FEE FUNDING MODEL

In the late 1980s, it took the FDA twenty-nine months to approve new branded drugs, and industry wanted a faster timeline.<sup>39</sup> To allow the FDA to hire more staff and approve drugs more quickly, the branded drug industry agreed to pay the FDA user fees for its drug approval applications.<sup>40</sup> The Prescription Drug User Fee Act ("PDUFA") was enacted in 1992 with agreements between the FDA, the branded drug industry, and Congress.<sup>41</sup> PDUFA promised improved approval times in exchange for industry funding.<sup>42</sup> The agreement contained assurances that fee funding would only be used "for activities to support the review of human drug applications and would supplement—rather than replace—funding that Congress appropriated to [the] FDA."<sup>43</sup>

PDUFA included a provision requiring reauthorization every five years.<sup>44</sup> Funding from industry took pressure off Congressional appropriations to the FDA.<sup>45</sup> For example, between 2012 and 2016, congressionally appropriated funding for the FDA increased by 9%, but the amount of money that industry paid the FDA as user fee funding increased over 50%.<sup>46</sup> Since the FDA relies so heavily on this funding for its operations and funding reauthorizations have to be negotiated with industry every five years to keep the funds flowing, the branded drug industry gained significant leverage to set the FDA's priorities every five years.<sup>47</sup> By 2016, "user fees account[ed] for 42%" of the FDA's total funding.<sup>48</sup> Donald Light, Joel

37. Hamburg, *supra* note 1, at 1-2.

38. THAUL & JOHNSON, *supra* note 27, at 3 (citing U.S. GOV'T ACCOUNTABILITY OFF., GAO-12-371R, *supra* note 25).

39. SUSAN THAUL, CONG. RESEARCH SERV., RL33914, THE PRESCRIPTION DRUG USER FEE ACT: HISTORY THROUGH THE 2007 PDUFA IV REAUTHORIZATION 1 (2008).

40. *Id.* at 2.

41. O'Leary, *supra* note 15, at 241.

42. *Id.*

43. THAUL & JOHNSON, *supra* note 27, at 1.

44. See Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. 46,929, 46,929-30 (July 19, 2016); *Prescription Drug User Fee Act (PDUFA)*, U.S. FOOD & DRUG ADMIN. (last updated Feb. 26, 2018), <https://www.fda.gov/ForIndustry/UserFees/Prescription-DrugUserFee/>.

45. See Light et al., *supra* note 2, at 595.

46. AGATA DABROWSKA & SUSAN THAUL, CONG. RESEARCH SERV., R44576, FOOD & DRUG ADMIN. BUDGET: FACT SHEET 2 (2016).

47. See Light et al., *supra* note 2, at 595.

48. DABROWSKA & THAUL, *supra* note 46, at 3.



Lexchin, and Jonathan Darrow suggested in the *Journal of Law, Medicine & Ethics* that “cultural capture of rhetoric about saving lives by getting new [branded] drugs to patients more quickly” tilts the balance of power toward the manufacturers in these negotiations.<sup>49</sup>

The generic drug industry is described as a fiercely competitive, low-profit-margin market that “is certainly not for sissies.”<sup>50</sup> In *The New York Times*, Charles Ornstein and Katie Thomas recently explained that “[a]mid all the public fury over the escalating costs of brand-name medications, the price of generic drugs has been falling, raising fears about the profitability of major generic manufacturers.”<sup>51</sup> One study showed manufacturers “make about three times the gross profits on branded [versus] generic drugs.”<sup>52</sup> The top five generic companies are the only companies that hold market shares above 5%.<sup>53</sup> Because profits in the generic drug industry are much thinner, the generic drug industry would benefit from the ability to lean on insurer contributions to its FDA approval application costs. Further, because there are fewer advocates for generic drugs—likely because the generic industry has fewer resources to fund patient groups and lobbyists—emphasizing the public health impact of generic drugs and involving the public health community in this advocacy would help establish generic drugs as an important constituency for the FDA.

Furthermore, the United States relies on generics to provide savings in the health system. A report by the Commonwealth Fund on high health care spending in the United States found that “prices for generic drugs are lower in the U.S. than in these other countries, whereas prices for brand-name drugs are much higher.”<sup>54</sup> This pricing inversion makes it difficult for the generic industry to take advantage of the user fee funding model because their profits are already so low.

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49. Light et al., *supra* note 2, at 595.

50. Eric Palmer, *Top 20 Generics Companies by 2014 Revenue*, FIERCEPHARMA, <http://www.fiercepharma.com/special-report/top-20-generics-companies-by-2014-revenue> (last visited Mar. 8, 2018).

51. Charles Ornstein & Katie Thomas, *Generic Drug Prices Are Falling, but Are Consumers Benefiting?*, N.Y. TIMES (Aug. 8, 2017), <https://www.nytimes.com/2017/08/08/health/generic-drugs-prices-falling.html?smid=tw-nythealth&smtyp=cur>.

52. Sood et al., *supra* note 21 (noting the authors’ perspective that the disparity was consistent with the patent protection branded drugs enjoy).

53. Palmer, *supra* note 50.

54. DAVID A. SQUIRES, EXPLAINING HIGH HEALTH CARE SPENDING IN THE UNITED STATES: AN INTERNATIONAL COMPARISON OF SUPPLY, UTILIZATION, PRICES, AND QUALITY, 5 (2012), [http://www.commonwealthfund.org/~media/files/publications/issue-brief/2012/may/1595\\_squires\\_explaining\\_high\\_hlt\\_care\\_spending\\_intl\\_brief.pdf](http://www.commonwealthfund.org/~media/files/publications/issue-brief/2012/may/1595_squires_explaining_high_hlt_care_spending_intl_brief.pdf).

### III. THE PROMISE OF FEE FUNDING FOR GENERICS

The FDA's branded drug user fee funding program ran for twenty years before generics received a similar program.<sup>55</sup> The branded drug funding program is known as PDUFA, and its counterpart for generic drug approvals is known as GDUFA.<sup>56</sup>

PDUFA's five reauthorizations have progressed smoothly, establishing significantly faster review times and establishing extensive communication and coordination between the FDA and the branded drug industry.<sup>57</sup> PDUFA I and II created a set of expectations industry could rely on in communications with regulators, and PDUFA III increased base user fees to create a sustainable funding structure and post-market surveillance procedures.<sup>58</sup> PDUFA IV featured another increase in funding, guidance for industry on new models of clinical trials, and extension of post-market surveillance.<sup>59</sup> PDUFA V created a formal structure of communication during review of applications with multiple interactions between the FDA and industry.<sup>60</sup> One might have imagined GDUFA could build on this established framework and hit the ground running. But that is not what happened.

GDUFA was first authorized in 2012, and many hoped that user fee funding for generics would help combat high drug prices by reducing the generic approval backlog at the FDA.<sup>61</sup> Commissioner Margaret Hamburg stated the "FDA was drowning in generic applications that arrive at the rate of almost 1,000 a year, pushing the backlog of ANDAs above 2,500, and stretching the median time for generic drug approvals to 31 months" before

55. *Protecting the Public Health: Examining FDA's Initiatives and Priorities - Hearing on Examining the FDA's Initiatives and Priorities, Focusing on Protecting the Public Health Before the S. Comm. on Health, Educ., Labor, & Pensions*, 113th Cong. 8 (2014) (statement of Comm'r Margaret A. Hamburg, M.D., U.S. Food & Drug Admin.).

56. O'Leary, *supra* note 15, at 245–46.

57. Jacqueline G. Lampert & David Kendall, *Ten Things You Need to Know About the FDA User Fee Reauthorizations*, THIRD WAY, §§ 7-8 (Apr. 20, 2017), <http://www.thirdway.org/primer/ten-things-you-need-to-know-about-the-fda-user-fee-reauthorizations> (explaining the reauthorization process, including the fact that the user fee programs are written with provisions requiring reauthorization of the user fee programs every five years).

58. Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. 46,929, 46,931 (July 19, 2016).

59. *Id.*

60. *Id.*

61. Zachary Brennan, *Generic Drug Backlog at FDA: A Dive into the Confusing Numbers*, REG. AFE PROF. SOC'Y (Nov. 1, 2016), <http://www.raps.org/Regulatory-Focus/News/2016/11/01/26106/Generic-Drug-Backlog-at-FDA-A-Dive-Into-the-Confusing-Numbers/>; *Prioritizing Public Health: The FDA's Role in the Generic Drug Marketplace: Hearing Before the Subcomm. on Agric., Rural Dev. & Fed. Drug Admin., & Related Agencies of the S. Comm. on Appropriations* (2016) (statement of Janet Woodcock, Director, Ctr. for Drug Evaluation & Research, USDA), <https://www.fda.gov/NewsEvents/Testimony/ucm522119.htm>.

the FDA took in user fee funding from generic drugs.<sup>62</sup> The FDA hoped GDUFA I would “ensure consumers continue to receive the significant benefits offered by generic drugs which provided more than \$824 billion dollars in savings to the nation’s health care system in the last decade alone” and reduce the expense of bringing products to market, thereby reducing costs to patients and payors.<sup>63</sup> A number of very costly drugs, earning over \$1 billion in revenue per year such as Singulair, the asthma medication, would lose their patent eligibility by 2015, contributing to the hope that the new generic fee funding program would allow generics to quickly provide a less costly alternative for these drugs.<sup>64</sup>

#### IV. THE FDA BEGINS ACCEPTING USER FEE FUNDING FOR GENERIC DRUGS

The Food and Drug Administration Safety and Innovation Act, the 2012 reauthorization of the FDA user fee programs and updates to FDA practices, included the inaugural version of GDUFA and became law on July 9, 2012.<sup>65</sup> Collecting user fees for generic drugs would allow the FDA to begin clearing the buildup of pending unacknowledged or unapproved generic drug applications. In GDUFA I, the FDA agreed to act on 90% of generic drug applications (“ANDAs”) that were submitted in 2017 within ten months.<sup>66</sup>

However, for generic applications in the “backlog,” specifically those applications submitted prior to July 9, 2012, the FDA only committed to take a first action on 90% of them by the end of 2017.<sup>67</sup> These backlogged applications did not receive “goal dates” by which a manufacturer can expect the FDA to have acted on its application.<sup>68</sup> Even if the FDA’s first action on any of these application asked the manufacturer to amend the application, that new submission still did not receive a goal date, creating an unpredictable and frustrating process.<sup>69</sup> ANDAs submitted in 2013 and 2014 also did not receive goal dates, and the FDA only committed to “maintain

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62. Hamburg, *supra* note 1, at 3.

63. FOOD & DRUG ADMIN., GDUFA COMMITMENT LETTER: HUMAN GENERIC DRUG PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2013 THROUGH 2017 1–2 (2012), <http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf>.

64. U.S. GOV’T ACCOUNTABILITY OFF., GAO-12-371R, *supra* note 25, at 2 n.8.

65. *Protecting the Public Health*, *supra* note 55, at 8.

66. GDUFA II LETTER, *supra* note 14, at 4.

67. Generic Drug User Fees: Request for Comments, 81 Fed. Reg. 66,035, 66,036 (Sept. 26, 2016).

68. See GDUFA II LETTER, *supra* note 14.

69. See Generic Drug User Fees: Request for Comments, 81 Fed. Reg. 66,035, 66,036.

pre-GDUFA levels of productivity.”<sup>70</sup> The lack of deadlines delayed progress while incoming applications mounted.

GDUFA’s struggle to improve productivity starkly differs from the initial changes brought about by PDUFA. Approval times for branded drugs quickly reduced after PDUFA first became law in 1993.<sup>71</sup> PDUFA I’s goal was to reduce median application review “from 27 months in FY 1993 to 12 months in 1998.”<sup>72</sup> The new funding for PDUFA I allowed the FDA to hire more review staff, and the FDA well exceeded PDUFA I’s goal, reducing review times to six months by 1998.<sup>73</sup>

This marked variation between the initial success of PDUFA and GDUFA might be traced to the fact that efforts to reduce approval times for generic drugs started at even more of a deficit. During negotiations for the initial GDUFA, median application review times for generic applications averaged thirty-one-months and had to compete with 2,500 backlogged applications.<sup>74</sup>

While PDUFA was able to reduce approval times for branded drugs, after GDUFA I was enacted, the approval delays for generic drugs actually lengthened. According to the Association for Accessible Medicines,<sup>75</sup> median ANDA approval time increased to between forty-eight and fifty months in 2015, amid an increasing backlog of pending requests.<sup>76</sup> Only about 1,550 generics were approved between 2013 when the FDA started taking in GDUFA I funding and 2016.<sup>77</sup> Some of the generics awaiting approval in 2012 were not considered part of the official backlog.<sup>78</sup> They were excluded from the backlog total because the FDA asked the manufacturer for an amended application or took a similar action.<sup>79</sup> Critics suggest

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70. *Id.*

71. THAUL & JOHNSON, *supra* note 27, at 1.

72. *Id.* at 1.

73. *Id.* at 3.

74. *Id.* at 5.

75. The Association for Accessible Medicines is the primary trade group for generic and biosimilar manufacturers and was known as the Generic Pharmaceutical Association until February 14, 2017. *Generic and Biosimilar Manufacturers Launch New Brand & Campaign to Expand Access to Medicines*, PR NEWSWIRE (Feb. 14, 2017), <https://www.prnewswire.com/news-releases/generic-and-biosimilar-manufacturers-launch-new-brand—campaign-to-expand-access-to-medicines-300406969.html>.

76. Generic Pharmaceutical Association, Comment Letter on Generic Drug User Fees 6 (July 15, 2015), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0023>.

77. Sydney Lupkin, *EpiPen Controversy Fuels Concern Over Generic Drug Approval Backlog*, KAISER HEALTH NEWS (Sept. 6, 2016), <http://khn.org/news/epipen-controversy-fuels-concerns-over-generic-drug-approval-backlog/>.

78. *Id.*

79. Lupkin, *supra* note 77 (quoting an FDA statement that “[m]ost applications from the backlog will need to come back to FDA for additional review due to deficiencies in the

that the exclusion of these rejected applications meant that in late 2016, “the agency [had] only approved about half the backlogged generics that were awaiting approval in 2012.”<sup>80</sup> The FDA made some headway, but “a flood of new applications . . . steadily added to the demand.”<sup>81</sup>

The FDA set the amount of money it would collect from industry participants in GDUFA I based on projections that industry would submit 750 ANDAs per year because ANDAs are “the primary workload driver of the program.”<sup>82</sup> However, the FDA received an average of 1000 applications per year over the first four years.<sup>83</sup> According to one industry participant, four years after GDUFA I, the FDA “ha[d] not yet fully staffed its inspection teams to adequately inspect the numerous facilities responsible for manufacturing generic [final dosage formulas] and [active pharmaceutical ingredients] for sale in the U.S.”<sup>84</sup> The FDA’s staff explained that facility inspections were delayed because of a lack of resources and expected “the percentage of inspections conducted to improve with additional funding from user fees from manufacturers of generic drugs.”<sup>85</sup> GDUFA II increased user fees by nearly \$200 million from about \$293 million annually in GDUFA I up to \$493 million annually in GDUFA II to account for the underestimation of its workload.<sup>86</sup>

Ensuring the FDA has sufficient funding to approve generic drug applications as quickly as possible has benefits across the healthcare system. Each day with no or few generic alternatives on the market means an additional day where patients, insurers, and the government pay high branded drug prices. The Association for Accessible Medicines cited a survey of its members estimating \$3.7 billion lost in healthcare savings “due to first ge-

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submissions.”); Ed Silverman, *FDA Still Struggling with Backlog of Generic Drug Applications*, STAT (Mar. 2, 2016), <https://www.statnews.com/pharmalot/2016/03/02/fda-generic-drugs/> (noting figures where FDA framed success as first review of an application, instead of approvals).

80. Lupkin, *supra* note 77.

81. *Id.*

82. FOOD & DRUG ADMIN., GDUFA II FEE STRUCTURE SUMMARY 1 (2016), <http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525236.pdf>.

83. *Id.*

84. Breckenridge Pharmaceutical, Inc., Comment Letter on Docket No. FDA-2012-N-0882: Generic Drug User Fees, 2 (Nov. 16, 2016), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0057>.

85. DEP’T OF HEALTH & HUMAN SERV.’S OFFICE OF INSPECTOR GEN., OEI-01-13-00600, FDA HAS MADE PROGRESS ON OVERSIGHT AND INSPECTIONS OF MANUFACTURERS OF GENERIC DRUGS 10 (May 2015).

86. Zachary Brennan, *GDUFA II Performance Goals: 8-Month Priority Reviews*, REG. AFF. PROF. SOC’Y (Oct. 17, 2016), <http://www.raps.org/Regulatory-Focus/News/2016/10/17/26013/Updated-GDUFA-II-Performance-Goals-8-Month-Priority-Reviews-More-Timely-Correspondence/>.

neric approval delays.”<sup>87</sup> Because the 180-day exclusivity period is a critical revenue window for the first generic maker on the market under the Hatch-Waxman Act, any approval delay is costly for the generic manufacturer as well.<sup>88</sup>

The FDA has made significant progress in generic drug approval over the last two years and has “met or exceeded all performance goals” announced in the original GDUFA Commitment Letter,<sup>89</sup> and the FDA under Commissioner Scott Gottlieb has taken interesting steps to improve generic drug competition with branded drugs.<sup>90</sup> To help ensure these improvements persist, the FDA should help identify the particular generic drugs that would drive the biggest public health impact and systemic savings. Identifying these drugs would demonstrate the incentive for insurers to sponsor applications for more generic competition for those drugs.

## V. PROPOSALS TO FIX THE SYSTEM

Some argue that funding the FDA “entirely . . . by taxpayers-as-consumers” is the only way for the agency to be truly accountable to the country’s interests.<sup>91</sup> If funding comes from the entire country’s tax base and is appropriated by Congress according to the spectrum of constituent needs, the agency will be funded by a more balanced and public-interest-minded set of interests in comparison to the self-serving interests driving industry funding. Professor Gilhooley recommends “at a minimum, limiting user fee support to half of the cost of the drug approval program, with the rest coming from government appropriations.”<sup>92</sup>

Professor Sharona Hoffman, who focusses on drug shortages in the generic market, calls for expanding the FDA’s public health powers to shape the market,<sup>93</sup> suggesting public health laws adopted to fight pandemics and natural disasters could provide a model for legislation allowing the FDA to

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87. See Generic Pharmaceutical Association, *supra* note 76, at 7.

88. See, e.g., Eisenberg & Thomas, *supra* note 24, at 9; Generic Drug User Fees: Request for Comments, 81 Fed. Reg. 66,035, 66,037 (Sept. 26, 2016).

89. *Hearing on Generic Drug User Fee Amendments: Accelerating Patient Access to Generic Drugs Before the S. Comm. On Health, Educ., Labor, & Pensions*, 114th Cong. (2016) (testimony of Janet Woodcock, M.D., Dir. of the Ctr. for Drug Evaluation & Research, U.S. Food & Drug Admin.).

90. Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access, Request for Comments, 82 Fed. Reg. 28,495 (June 22, 2017). See *infra* Sec. VI.A.1 for a discussion of the FDA’s recent steps.

91. Light et al., *supra* note 2, at 597.

92. Gilhooley, *supra* note 8, at 329–30.

93. Sharona Hoffman, *The Drugs Stop Here: A Public Health Framework to Address the Drug Shortage Crisis*, 67 FOOD & DRUG L.J. 1, 12–13 (2012).

place requirements on the generic industry to avoid shortages.<sup>94</sup> She suggests penalizing manufacturers who do not keep up with demand and cause shortages, and rewarding manufacturers who meet demand during drug shortages.<sup>95</sup> While that proposal may be effective in the short-term or in relation to a specific shortage crisis, penalizing manufacturers that are struggling to produce sufficient drug quantities would likely remove resources from the comparatively under-resourced generics industry.<sup>96</sup> Adding funding from ‘sponsors’ and potentially boosting Congressional appropriations as a response to public health engagement can do more to both alleviate shortages and improve drug access. Sufficient Congressional appropriations, though not always stable and reliable, would be ideal, but the fee-funding model is becoming entrenched, having expanded to other FDA programs.<sup>97</sup>

Therefore, creating another funding stream to support generic drug approval at the FDA would have the advantage of both allowing FDA to hire more staff focused on generics and create more sophisticated processes to ensure rapid approvals. Another funding stream would also allow later GDUFA negotiations to focus on applying the achievements and structures from PDUFA to the generic approval process instead of being consumed by disputes among generic industry participants over the division of user fee obligations within the industry. Creating another funding stream should be accomplished in three steps: 1) identifying the most effective place to target those funds 2) creating a formal program to direct the funds’ use, and 3) codifying the FDA’s new efforts to ask public health stakeholders to identify additional barriers to effective generic drug development and approval.

First, the FDA should conduct a biennial series of studies of medication adherence,<sup>98</sup> health outcomes, and overall cost of care based on generic availability for specific drugs widely used by vulnerable patient populations with chronic conditions. This study can be used to identify branded drugs that are most in need of generic alternatives.

This proposal was inspired by an article written by Professor Margaret Gilhooley, a former attorney in the FDA’s Office of Chief Counsel and a retired Professor of Law at Seton Hall Law School.<sup>99</sup> Professor Gilhooley’s

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94. *See id.* at 12–16.

95. *See id.* at 13, 17.

96. Ornstein & Thomas, *supra* note 51.

97. Lampert & Kendall, *supra* note 57.

98. Medication adherence is a measure of whether patients take medication as prescribed by their medical providers, without skipping or reducing doses. *See, e.g.*, Kesselheim & Darrow, *supra* note 3, at 295 n.6.

99. Gilhooley, *supra* note 8, at 327 (calling for a study to determine “the extent to which public health has improved because of the faster approval of drugs made possible by the user fee system”).

idea of tying drug approval timelines to public health impact is particularly critical for generics used by low-income patients with chronic conditions. In combination with this narrowed focus on this vulnerable and costly population and two additional steps, (1) insurer support for fee funding and (2) engagement with the public health community, the FDA can ensure a successful and sustainable generic drug approval program going forward.<sup>100</sup>

These proposed studies will build on earlier research<sup>101</sup> to pinpoint brand drugs where generic competition would serve a triple aim: helping vulnerable patient populations achieve better health by being less likely to skip costly prescribed medications, save the healthcare system money by reducing preventable negative outcomes from improperly treated chronic conditions, and save insurers money in providing drug coverage. Patient failure to take medication as prescribed can lead to negative outcomes like “stroke in hypertensive patients, higher viral load in patients with HIV, and hospitalization and mortality in patients with heart failure.”<sup>102</sup> Treatment for these negative outcomes is significantly more resource-intensive than adhering to the prescribed medication regimen and leads to increased costs across the health system.<sup>103</sup> Identifying the drugs patients are most likely to skip or take at a reduced dose because of cost and the resulting systemic outcomes will highlight specific drugs where lowered cost through adding generic alternatives will do the most good.

Second, Congress should amend Title III of the FDA Reauthorization Act of 2017 (“GDUFA II”) to allow insurers to sponsor generic entry for drugs that the proposed studies show improve health outcomes for vulnerable populations. Sponsored drugs that meet these standards would qualify for priority review as defined by the FDA’s Center for Drug Evaluation and Research.<sup>104</sup> This amendment could take the FDA’s findings from its current generic outreach efforts in combination with these proposals and incorporate them into the 2022 reauthorization of the FDA’s user fee

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100. *Id.* at 329.

101. *See, e.g.*, Rector & Venus, *supra* note 18, at 219 (finding cost-related medication nonadherence among elderly adults with chronic conditions); Public Citizen, Comment Letter on Administering the Hatch-Waxman Amendments (Sept. 19, 2017), <https://www.regulations.gov/document?D=FDA-2017-N-3615-0078> (describing a study that found the U.S. ranked worst out of eleven developed countries for medication nonadherence based on cost).

102. Kesselheim & Darrow, *supra* note 3, at 316

103. *Id.* (explaining that medication nonadherence may cost the U.S. health system more than \$100 billion per year “due to complications that could have been prevented.”).

104. CTR. FOR DRUG EVALUATION & RESEARCH, MANUAL OF POLICIES AND PROCEDURES, 5240.3 REV. 3-4, “PRIORITIZATION OF THE REVIEW OF ORIGINAL ANDAs, AMENDMENTS AND SUPPLEMENTS” (2017). The Center for Drug Evaluation and Research is the division of the FDA that is primarily responsible for drug approval.



programs.<sup>105</sup> Generic drugs need both credit for the public health impact of medication affordability and supplemental funding to achieve FDA review parity with pioneer drugs. The proposed study provides the public health impact data and the supplemental insurer funding provides the needed support to help generics target the branded drugs where competition is most needed.

Third, generic drugs need additional engagement from public health and consumer advocates, insurers, and others with incentives to reduce costs in the system. Recent FDA initiatives to seek input on improving generic drug availability have generated enthusiastic responses.<sup>106</sup> When the FDA held a public meeting on these issues on July 18, 2017, the Agency received input from a wide variety of healthcare providers, legal experts, independent patient advocates, and public health advocates.<sup>107</sup> Amending the procedures for generic user fee reauthorization to require the FDA to seek comment from these groups each time GDUFA is reauthorized will, in combination with the additional funding, support an effective, medication-access-oriented program of generic approval at the FDA.

## VI. RECENT DEVELOPMENTS

Both PDUFA and GDUFA were recently reauthorized in August 2017.<sup>108</sup> Reauthorizing these programs follows a series of similar steps. First, after extensive negotiations between the FDA and industry, as well as meetings with stakeholders, the FDA summarizes the negotiated agreements in documents called Commitment Letters.<sup>109</sup> The FDA then holds a public meeting to review the Commitment Letters and opens the letters for

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105. This amendment would most logically come as part of the reauthorization of the FDA's user fee programs in 2022 but certainly, the earlier the better. *See supra* Section II for a discussion of the regular reauthorization of FDA user fee programs.

106. Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access, Request for Comments, 82 Fed. Reg. 28,493 (June 22, 2017). Interestingly, these responses included few disease-specific patient advocate groups, which supports an inference that these disease-specific groups are most typically aligned with and funded by branded drug manufacturers. *See* Katie Thomas, *More than 80 Percent of Patient Groups Accept Drug Industry Funds*, N.Y. TIMES (Mar. 1, 2017), <https://www.nytimes.com/2017/03/01/health/patient-groups-drug-industry-money.html>.

107. Administering the Hatch-Waxman Amendments, 82 Fed. Reg. at 28,493.

108. FDA Reauthorization Act of 2017, 21 U.S.C. §§ 292-393 (2012). This legislation includes the sixth reauthorization of PDUFA (PUDFA VI, Title I of the legislation) and the second reauthorization of GDUFA (GDUFA II, Title III of the legislation).

109. *GDUFA Reauthorization Public Meetings*, FOOD & DRUG ADMIN., <http://wayback.archive-it.org/7993/20170721224529/https://www.fda.gov/ForIndustry/UserFees/GenericDrug/UserFees/default.htm> (last visited Mar. 8, 2018); *Prescription Drug User Fee Act (PDUFA)*, FOOD & DRUG ADMIN. (2017), <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrug/UserFee/default.htm>.

public comment.<sup>110</sup> After reviewing comments from negotiators, stakeholders, and the public, the FDA submits the Commitment Letters to Congress to accompany legislation.<sup>111</sup>

Based on a review of comments related to those most recent public meeting, the Commitment Letters and comments for each program's upcoming reauthorization suggest disparities between the generic and branded programs. While part of GDUFA's struggle to achieve PDUFA's rapid reductions in review times may be because it is a new program, tight funding in the generic industry and failure by industry, public health stakeholders, and the FDA to focus on the public health benefits of generics have created a serious discrepancy between the two programs.

## A. GDUFA II

### 1. Reauthorization Provisions

Discussions between the FDA and industry for GDUFA II focused on addressing GDUFA I's immediate problems, such as making submission review performance goals more specific, improving communication between the FDA and industry while ANDAs are under review, and structuring the fee-funding schedule to better reflect the generic market structure while allowing the FDA to raise more revenue.<sup>112</sup> Leading up to the publication of the Commitment Letter that set out the FDA's agreements with industry on topics including how user fees will be structured and the communications protocols between the FDA and industry for pending generic drug applications, the FDA held two public meetings, eight meetings with stakeholders, and over twenty-five meetings with industry.<sup>113</sup>

The GDUFA II Commitment Letter focuses on review times, communication between the FDA and industry, manufacturing facility inspection, and adjusting the balance of fees between participants in the generic industry.<sup>114</sup> The FDA will scrap the tiered goal-date formula that caused trouble in GDUFA I and set standard ANDA review times at ten months.<sup>115</sup> Priority review will be completed within eight months.<sup>116</sup> The priority review is contingent on complete facility information for manufacturing and testing

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110. *GDUFA Reauthorization Public Meetings*, *supra* note 109; *Prescription Drug User Fee Act*, *supra* note 109.

111. *GDUFA Reauthorization Public Meetings*, *supra* note 109; *Prescription Drug User Fee Act*, *supra* note 109.

112. Generic Drug User Fees: Request for Comments, 81 Fed. Reg. 66,035, 66,036-37 (Sept. 26, 2016).

113. *GDUFA Reauthorization Public Meeting*, *supra* note 109.

114. Generic Drug User Fees: Request for Comments, 81 Fed. Reg. at 66,036-38.

115. *Id.* at 66,036.

116. *Id.*

facilities because this “frequently impact[s] ANDA approvability.”<sup>117</sup> These basic issues of approved manufacturing and testing facilities speak to the low profit margins and fragmentation among industry participants.

Just before Congress passed GDUFA II as part of the FDA Reauthorization Act of 2017, the FDA made two important regulatory changes to promote generic competition with branded drugs. First, the FDA published a list of branded drugs that no longer had patent or regulatory exclusivity and still had no approved generic competitor, making it easier for generic drug makers to identify drugs to produce.<sup>118</sup> Second, the FDA assigned priority review to generic applications for drugs with fewer than three generic competitors when priority review had previously only been available for the first generic competitor.<sup>119</sup> The FDA also announced a public meeting to solicit feedback on ways the legal framework around regulatory and patent exclusivities have been used inappropriately to delay generic competition and received a significant volume of feedback.<sup>120</sup> These changes make it easier for generic drug manufacturers to identify branded drugs that need competition and pave the way for more prompt approval of those competitors. In combination with the additional funding and more frequent communication between the FDA and industry in GDUFA II, these changes could go a long way to increasing generic competition in the drug market.

GDUFA II included important improvements from GDUFA I, including increased fees and improved communication between the FDA and the generic industry. Fees increase significantly in GDUFA II from about \$300 million per year to \$493.6 million.<sup>121</sup> The increase is in part to compensate for the FDA’s under-estimation of the number of ANDAs that it would be expected to handle each year in GDUFA I.<sup>122</sup> The relative distribution of responsibility for fee funding is naturally a central issue in the reauthorization. It reveals market tightness and supports the need for additional user fee support from outside sources, particularly insurers, who have a financial incentive to support lower drug prices.<sup>123</sup> For GDUFA II, the “FDA and

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117. *Id.*

118. *FDA Tackles Drug Competition to Improve Patient Access*, FOOD & DRUG ADMIN. (June 27, 2017), <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm564725.htm>.

119. *Id.*

120. Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access, Request for Comments, 82 Fed. Reg. 28,493 (June 22, 2017).

121. Brennan, *supra* note 86.

122. *Id.*

123. See, e.g., Breckenridge Pharmaceuticals, *supra* note 84 (objecting to the GDUFA II proposal to shift more user fees from generic manufacturing facilities to ANDA-holders: entities which lead the applications for FDA approval).

industry have agreed to shift the burden more toward annual program fees[,]” instead of application fees, to smooth revenue between years and “[m]ore closely align fee responsibility with program costs and fee-paying ability.”<sup>124</sup> The issue with fee-paying ability is not, as with pioneer drugs, the threat that the companies will put less into research, development, and advertising. Instead, for generics, it is more about whether generic manufacturers will be able to stay in business at all under these increased fees.<sup>125</sup> Allowing insurers to contribute user fees will offset some of this pressure.

Communication between the FDA and generics manufacturers during the application process is much less extensive than between the FDA and branded drug manufacturers. Branded drug-makers have “a path to approval that allow[s] them to make adjustments at every stop along the way,”<sup>126</sup> while generic drug-makers risk losing their approval timeline when the FDA requests an amendment to an application.<sup>127</sup> GDUFA I attempted to improve communication between industry and the Agency through the approval process, keeping industry advised of problems that could be easily fixed.<sup>128</sup> However, “[t]hese enhancements, as operationalized, did not meet industry’s expectations and were reportedly commercially disruptive.”<sup>129</sup> In GDUFA II, the FDA will determine whether to accept an ANDA for review within 60 days of submission and within that time period, give applicants a quick-turnaround opportunity to make corrections.<sup>130</sup> In GDUFA II, the FDA committed to continue work through the deadline it set for response to the generic drug maker if the continued work would “likely result in an imminent tentative approval that could prevent forfeiture of 180-day exclusivity or an imminent approval.”<sup>131</sup>

These improvements are important steps to achieving parity between the generic and branded drug programs at the FDA. When combined with additional user fee funding from insurers and sustained engagement from public health advocates, the FDA will be primed to make a significant contribution in reducing costs and improving outcomes in the American health-care system by taking full advantage of generic drugs’ potential.

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124. See *Protecting the Public Health*, *supra* note 55.

125. Ornstein & Thomas, *supra* note 51 (describing earnings difficulties in the generic industry).

126. Lampert & Kendall, *supra* note 57, at § 4.

127. Lupkin, *supra* note 77.

128. Generic Drug User Fees: Request for Comments, 81 Fed. Reg. 66,035, 66,037 (Sept. 26, 2016).

129. *Id.*

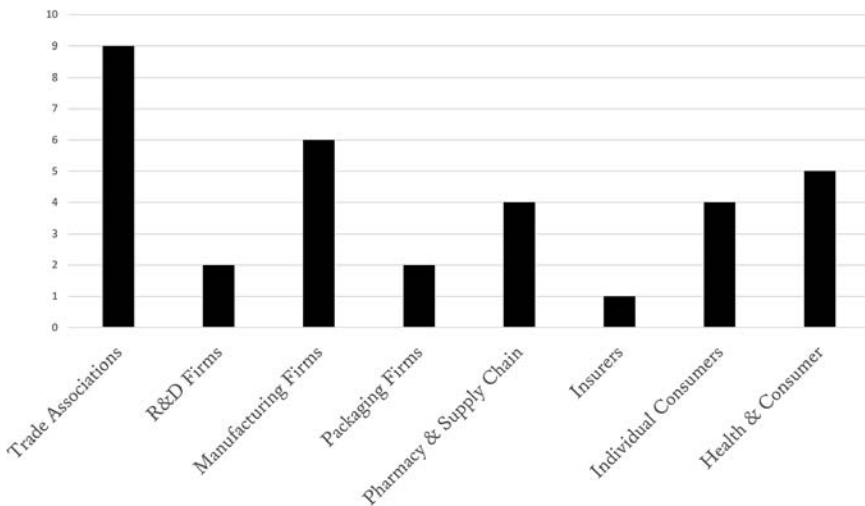
130. *Id.*

131. *Id.*

## 2. Comments

The identities of public commenters for the most recent GDUFA Commitment Letter demonstrate the fragmentation of the generics industry and the minimal engagement from the broader health system, particularly health advocacy groups.

FIGURE 1.<sup>132</sup> GDUFA II COMMENTS FROM PUBLIC MEETING ON COMMITMENT LETTER



Most comments focused on the balance of fees between different industry participants like manufacturers, packagers, and developers.<sup>133</sup> Some comments are from entities that package, manufacture, and develop generics only for a small number of drugs.<sup>134</sup> Others manufacture and package drugs but do not actually hold the approved generic application and believe the balance of fees tilts too heavily toward manufacturers and packagers and away from developers.<sup>135</sup> There are no strong constituencies of patient groups and provider groups pushing the GDUFA negotiators to consider public health or patient needs, as there is in PDUFA.<sup>136</sup> While it is unclear

132. Figure 1 is based on my categorization of comments submitted in response to Generic Drug User Fees: Request for Comments, 81 Fed. Reg. at 66,035.

133. Generic Drug User Fees: Request for Comments, 81 Fed. Reg. at 66,035.

134. *See, e.g.*, Hanford Pharmaceuticals, Comment Letter on Generic Drug User Fees (July 13, 2015), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0021>.

135. *See* Catalent Pharma Solutions, Comment Letter on Generic Drug User Fees (July 15, 2015), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0024>.

136. *Compare* Generic Drug User Fees: Request for Comments, 81 Fed. Reg. at 66,036 (containing five comments from health system and consumer groups), *with* Prescription

how this patient constituency developed for PDUFA, the branded drug industry is known to sponsor patient advocacy groups, particularly disease-specific groups.<sup>137</sup>

GDUFA II's goal to approve first generics as soon as possible was applauded in a comment from the pharmacy chain CVS.<sup>138</sup> Another comment from a small think tank argued that the Veterans Health Administration is challenged by "remarkable increases in cost in selected generic products" and expressed hope that faster generic approvals could help.<sup>139</sup> Overall, however, the perspectives of advocates for seniors (who tend to have higher medical needs), low-income communities, and affordable public health were missing from the comments. The FDA and Congress would benefit from hearing from additional public-health minded stakeholders about the need for improved generic approval times, just as they currently benefit from hearing from patient advocates for breakthrough therapies.

The only other major health care industry stakeholder engaging in the GDUFA II comment period was Kaiser Permanente, which emphasized that "[a]s the frequency of drug shortages has increased, the time for ANDA approvals has also increased."<sup>140</sup> Kaiser suggested "offering incentives in the form of fee waivers/discounts and/or fast-track approvals, for generic manufacturers to enter market segments most vulnerable to shortages."<sup>141</sup> Waiving fee funding may be effective to encourage submissions, but given that the FDA was not able to meet review goals under GDUFA I's lower funding scheme, reducing the amount of funding the FDA takes in by waiving fees will not significantly improve drug availability. Adding insurers as a funding source for review fees will help ensure the FDA receives the fee funding necessary to hire staff to improve communication with generic manufacturers on their applications, conduct facility inspections promptly, and review applications quickly.

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Drug User Fee Act: Request for Comments, 81 Fed. Reg. 46,929, 46,929-30 (July 19, 2016) (containing twenty-seven comments from health system and consumer or patient advocates).

137. Thomas, *supra* note 106.

138. CVS, Comment Letter on No. FDA-2012-N-0882 Generic Drug User Fees, 3 (Nov. 16, 2016), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0049>.

139. Center for Health Equity, Research, & Promotion, Comment Letter on Generic Drug User Fees No. FDA-2012-N-0882 (June 10, 2015), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0031>.

140. Kaiser Permanente, *Written Testimony of Dr. Sharon Levine on Generic Drug User Fee Amendments of 2012*, at 3 (July 15, 2015), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0025>.

141. *Id.* at 6.

## B. PDUFA VI

The PDUFA framework is far more detailed and extensive than the GDUFA framework. PDUFA has the advantage of a longer history, but it also benefits from the branded drug industry's ability to pay user fees sufficient to support extensive hiring at the FDA. The large stakeholder community that engages with the FDA during PDUFA reauthorizations also likely contributes to focusing the FDA's attention on branded drugs.

### 1. Provisions

The resource differential between the generic and branded drug industries is visible even in the format of the public comments submitted to the FDA during the Commitment Letter negotiation process. Nearly all branded drug companies' comments appear on letterhead, written by regulatory affairs teams or lobbyists, while some of the generic companies' comment are simply typed into the Regulations.gov submissions page without formal signatures.<sup>142</sup> The resource differential likely supported branded manufacturers' successful development of extensive communication protocols with the FDA during the application process, which provides numerous opportunities to correct or clarify applications<sup>143</sup> and has established rapid approval timelines that the FDA adheres to closely.

Although reviewing clinical trial data to assess new drugs for approval is significantly more complex than assessing bioequivalence and safe manufacturing for generics, PDUFA VI's performance goal for standard new drugs is ten months: the same as for standard generics.<sup>144</sup> The FDA's new approval goal for priority new drug applications is six months, two months faster than the less complex priority generic applications.<sup>145</sup>

The FDA held two public meetings, six meetings with stakeholder groups, and over fifty discussions with industry leading up to the most recent reauthorization.<sup>146</sup> Negotiators for industry and the FDA worked through fine details of the FDA-industry communication process and ham-

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142. Compare *ASTRAZENECA PHARMACEUTICALS LP, RESPONSE TO FDA REQUEST FOR COMMENTS, PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022* (Aug. 4, 2016), <https://www.regulations.gov/document?D=FDA-2016-N-1895-0002>, with Karen Vescovi, Comment Letter on Generic Drug User Fees No. FDA-2012-N-0882 (Oct. 20, 2016), <https://www.regulations.gov/document?D=FDA-2012-N-0882-0043>.

143. PDUFA LETTER, *supra* note 14, at 4.

144. *Id.* at 4; GDUFA II LETTER, *supra* note 14, at 5.

145. PDUFA LETTER, *supra* note 14, at 4; GDUFA II LETTER, *supra* note 14, at 5.

146. FOOD & DRUG ADMIN., PDUFA VI: FISCAL YEARS 2018-2022, <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm> (last visited Mar. 8, 2018).

mered out industry's push for "real world" evidence.<sup>147</sup> PDUFA VI features extensive procedural guidance for communication between branded drug makers and the FDA.<sup>148</sup> The Commitment Letter describes particular materials and issues to discuss at each step of the branded drug approval process, proposing that the communication cycle be formally set out between each applicant and review team.<sup>149</sup> For the fast track program applicable to breakthrough therapies, industry receives "intensive FDA guidance on an efficient drug development program, and an organization commitment by [the] FDA involving senior managers."<sup>150</sup>

The FDA proposes to add 230 full time staff to aid the branded drug review process over PDUFA VI at a cost of over \$75 million.<sup>151</sup> This massive increase in staff for branded drugs renders it unlikely that generic drugs will be able to compete effectively for the FDA's attention without supplementary resources like this Note proposes.

## 2. Stakeholders

The public comments on the most recent reauthorization of PDUFA reflect the broad stakeholder community that engages with the FDA to develop the branded drug approval program. Healthcare and patient advocates and providers have a substantial presence in the conversation as demonstrated by the volume of comments submitted.

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147. PDUFA LETTER, *supra* note 14, at 4.

148. *Id.*

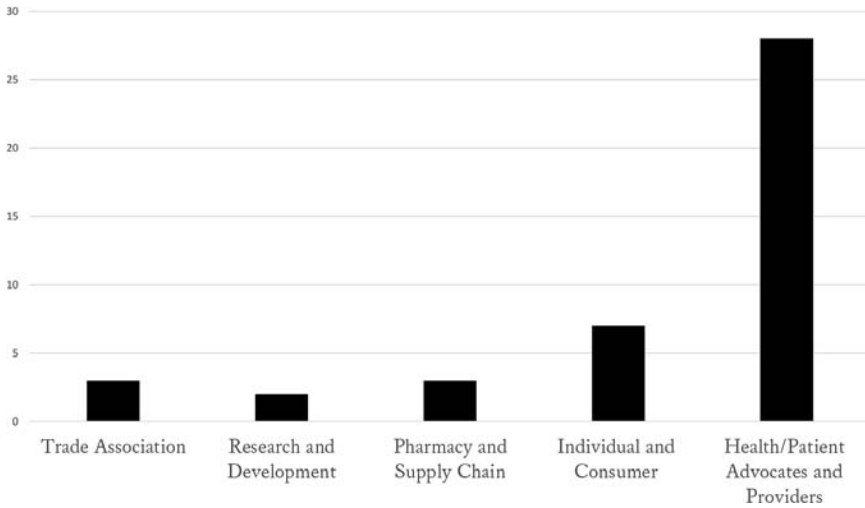
149. *Id.*; Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. 46,929, 46,929-30 (July 19, 2016).

150. PDUFA LETTER, *supra* note 14, at 22.

151. Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. at 46,934-35.



FIGURE 2.<sup>152</sup> PDUFA VI COMMENTS FROM PUBLIC MEETING  
ON COMMITMENT LETTER



The FDA receives significantly more engagement from patient advocates and health-focused groups when negotiating the branded drug approval program than when negotiating the generic drug approval program. Branded drugs are critical for patients suffering from conditions with few or no treatment options, which likely contributes to the patient-focused engagement in PDUFA. However, this engagement often aligns with branded drug research and manufacturing firms' interests, creating an additional source of pressure on the FDA to prioritize the branded drug review.<sup>153</sup>

One example of this effective coordination is the provision for “real-world evidence” in PDUFA VI, which draws united support from patient advocates and pioneer drug firms.<sup>154</sup> The FDA “proposes to conduct one or more public workshops” on how to gather and use “real-world” evidence in determining safety and effectiveness of medications.<sup>155</sup> Pharmaceutical Research and Manufacturers of America, the branded drug trade group, applauds the plan to use patient experiences and “patient-reported outcomes” to contribute to regulatory decision-making.<sup>156</sup> If the FDA was regularly hearing from a similarly broad and engaged base of stakeholders consist-

152. Figure 2 is based on my categorization of comments submitted in response to Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. at 46,929.

153. Thomas, *supra* note 106.

154. Prescription Drug User Fee Act: Request for Comments, 81 Fed. Reg. at 46,933.

155. *Id.*

156. Pharmaceutical Research and Manufacturers of America, Comment Letter on Docket No. FDA-2016-N-1895-0038: Prescription Drug User Fee Act; Public Meeting; Re-

ently pushing the agency to think about generic drugs and stay accountable to generic drug approval commitments, generic drugs will cement their status as equals to branded drugs within the FDA.

### CONCLUSION

A sustainably funded generic drug approval system that targets the most impactful generic drug approvals for funding would be valuable for under-resourced patient groups, the health system, the country as a whole, and particularly under-resourced communities. Delays in the FDA's reviews of generic drugs pose a significant risk to the public health, particularly now that many health insurance plans come with multi-thousand-dollar deductibles.<sup>157</sup>

The FDA's FAQs on drug approval includes "What can the FDA do about the cost of drugs?"<sup>158</sup> The FDA's provided answer is that the "FDA has no legal authority to investigate or control the prices charged for marketed drugs . . . [the] FDA recognizes that other factors beyond its purview, including insurance coverage and drug pricing, can determine patient access to drugs."<sup>159</sup> Adding insurer funding to support generic drug approval at the FDA would help the FDA improve patient access to drugs. Creating this additional funding stream would also allow the FDA to focus its generic drug program development on speed and efficiency, instead of balancing responsibility to pay fees among generic industry participants. The entire health system will benefit from three changes. First, the FDA must identify the drugs most in need of generic competition to promote medication adherence and avoid preventable complications and treatment. Second, insurer funding support will ensure user fees do not make it hard for those generic drugs to get to market. Finally, the FDA must be regularly reminded by an engaged stakeholder community that approving generic drugs quickly is just as important as approving branded drugs quickly.

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quest for Comments (Aug. 22, 2016), <https://www.regulations.gov/document?D=FDA-2016-N-1895-0038>.

157. Shefali Luthra, *Even With 'Skin in the Game,' Health Care Shoppers Are Not More Savvy*, KAISER HEALTH NEWS (Jan. 19, 2016), <http://khn.org/news/even-with-skin-in-the-game-health-care-shoppers-are-not-more-savvy/>.

158. *Frequently Asked Questions about CDER*, FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/FAQsaboutCDER/#16> (last visited Mar. 8, 2018).

159. *Id.*

