

FDA User Fees: Examining Changes in Medical Product Development and Economic Benefits

KEY FINDINGS

- The Food and Drug Administration (FDA) assesses and collects user fees to supplement Congressional appropriations. In fiscal year (FY) 2022, user fees represented 46% (\$2.9 billion) of FDA's total budget of \$6.2 billion.
- User fees vary substantially across FDA programs. In FY2022, across FDA's medical product centers, user fees accounted for \$1.4 billion (66%) of the human drugs program budget, \$197 million (43%) of the biologics program budget, and \$228 million (35%) of the medical device program budget.
- Research evidence suggests that user fees have contributed to increased access to new medical products for patients and reduced review timelines for industry. The benefits of user fees can be substantial for industry and patients.
- Using public and proprietary data from 2000 to 2018, we estimate that between 0.5% and 2.0% of the total cost of developing a new drug, complex medical device, or preventive vaccine went towards user fees. Using data from 2013 to 2021, we estimate that 1.7% of the total cost to develop a generic drug went towards user fees.

Introduction

The Food and Drug Administration (FDA) relies on funding from two sources to support its regulatory activities: user fees and budget appropriations and user fees paid by industry. Both sources of funding are authorized by Congress. FDA collects user fees from the regulated industry; for medical products, this includes biopharmaceutical and medical device companies. Budget appropriations are borne by the public more broadly through taxes, while user fees are directly supported by sponsors of medical product applications through reduced profit margins and indirectly borne by consumers to the extent that fees are passed through to consumers through increased prices. User fee programs are intended to supplement Congressional appropriations.

User fees for all human medical products, which includes prescription drugs, medical devices, generic drugs, and biosimilars, are reauthorized together on a five-year cycle. The reauthorization process begins with FDA and industry negotiating performance goals, such as completing reviews within a specified timeframe. As part of the reauthorization process, other relevant stakeholders also provide input on the draft agreement through public comment. FDA then transmits the final agreement to Congress for approval. On September 30, 2022, the President signed legislation reauthorizing the medical product user fees for an additional five years, through September 30, 2027.

The goal of this Issue Brief is to provide a primer on FDA user fees, present findings that examine how user fees affect the costs of medical product development, and summarize the research literature on user fees, most notably in expediting medical product development and approval.

History of User Fees

In the late 1980s, long FDA review times (on average 29 months) for human drug applications raised concerns from manufacturers that lengthy review times meant lost sales and from patient advocates about delayed access to new treatments.¹ This was particularly salient in part due to a backlog of applications for new antibiotics, drugs for heart failure, and therapeutics for the AIDS crisis.² Lengthy review times were primarily due to limited budgetary resources.

Another challenge was that sponsors lacked information about the status of their applications and predictability around their application review times; industry meetings with FDA were often considered a privilege because there were not enough resources to support even the required meetings.² In response, industry, with support from patient advocates, agreed to pay user fees beginning in 1992 to supplement the FDA budget in exchange for agreements to reduce review times. Since the 1950s, Federal agencies, including FDA, Congress, and the Courts, had deliberated about the merits and legality of user fees for federal programs. These discussions included the Office of Management and Budget's guidance on user fees issued in 1959, which specified that if the benefits of a good or service accrues broadly to the public, then the goods or services should be financed by taxes paid by the public.³ By the early 1980s a Supreme Court decision clarified aspects of user fee programs that opened the way for a user fee structure for federal agencies including FDA. The decision led to the eventual conclusion that as long as user fees were specifically structured with a "public health component" funded through budget authority and a "industry benefit" component funded through user fees, they would be legal.² By charging the costs of programs or activities to those that benefit the most from them, user fees can reduce taxpayer burden, while also reducing uncertainty for industry by giving them predictable and shorter review timelines.

To date, the authorizing legislation for each user fee program has set an amount of fee revenue for the first year of the program with annual adjustments for subsequent years, specified the types of fees that may be assessed and collected, and established legal conditions in order for FDA to collect user fees. It also has committed FDA to certain performance goals, such as completing reviews within a specified timeframe. Some of the user fee programs require reauthorization to continue while others are permanently authorized.⁴

Figure 1 shows FDA's budget from FY 1992 through FY 2020 and the relative portion of the budget that is made up of user fees versus budget authority. We see that FDA's budget has risen over time, with the greatest increases due to user fees, rather than increases in budget authority. Specifically, FDA's budget has grown from just under \$1 billion in FY 1992, when it was entirely budget authority, to almost \$6 billion in FY 2020, approximately \$3 billion of which was for user fees.

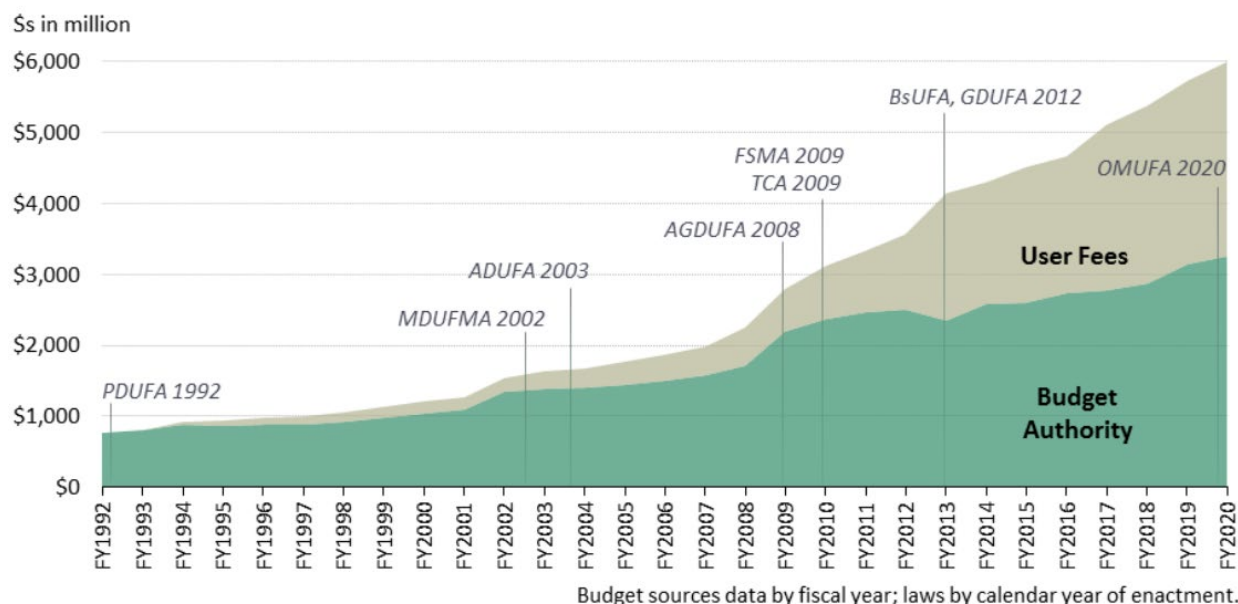
¹ Cutler, D.M. (2019). Extending the User Fee Approach to Pharmaceuticals. *The JAMA Forum*, 320(15): 1525-1526.

² Woodcock, J & Junod, S. PDUFA Lays the Foundation: Launching into the Era of User Fee Acts U.S. Food and Drug Administration. <https://www.fda.gov/files/about%20fda/published/PDUFA-Lays-the-Foundation--Launching-Into-the-Era-of-User-Fee-Acts.pdf>

³ Office of Management and Budget. (1993). Circular No. A-25 Revised. Memorandum for Heads of Executive Departments and Establishments, Available at: https://obamawhitehouse.archives.gov/omb/circulars_a025/; last accessed August 28, 2022.

⁴ For additional details on user fee programs and how they work, see the various Congressional Research Service reports on this topic. For example: Bodie, A. Sarata, A.K. FDA Human Medical Product User Fee Programs. Congressional Research Service, Report R44750, September 2021. Available at <https://crsreports.congress.gov/product/details?prodcode=R44750>.

Figure 1. Distribution of User Fees and Budget Authority for FDA, 1992-2020 (\$millions)



Budget sources data by fiscal year; laws by calendar year of enactment.

Source: This graph is reproduced from a report by the Congressional Research Service⁵

Figure 2 shows how user fees fit into the overall FDA budget. In fiscal year (FY) 2022, across FDA’s medical product centers, user fees made up approximately 46 percent (\$2.9 billion) of FDA’s total operating budget of \$6.2 billion.⁶ Focusing specifically on medical products, user fees accounted for \$1.4 billion (66 percent) of the human drugs program budget, \$197 million (43 percent) of the biologics program budget, and \$228 million (35 percent) of the medical devices program budget.⁶ User fees for prescription drugs, including biologics and generic drugs, and medical devices are the focus of this report; however, additional medical product user fee programs have also been authorized for biosimilars,⁷ over-the-counter drugs,⁸ animal drugs,⁹ and animal generic drugs.¹⁰ User fees also exist for the other products regulated by FDA, including tobacco products, which are funded entirely through user fees, and foods, which are funded almost entirely through budget authority.¹¹ The money collected through each of the user fee programs has specific allowable and excluded costs in terms of what FDA is allowed to spend the funds on. Allowable costs are for activities that directly relate to the respective user fee program (e.g., application review, regulatory research to support the submission of high-quality applications and reduce time to approval, facility inspections, and post-market safety surveillance), while excluded costs are all FDA actions that are not specific to the user fee programs, such as agency infrastructure and other agency wide efforts.

⁵ Congressional Research Service. (2022). The Food and Drug Administration (FDA) Budget: Fact Sheet. Report # R44576. <https://crsreports.congress.gov/product/pdf/R/R44576>

⁶ U.S. Food and Drug Administration. (2022). FDA At a Glance. <https://www.fda.gov/media/154548/download>

⁷ Biosimilar User Fee Act “BsUFA” began in 2012. <https://www.fda.gov/industry/fda-user-fee-programs/bsufa-authorization>

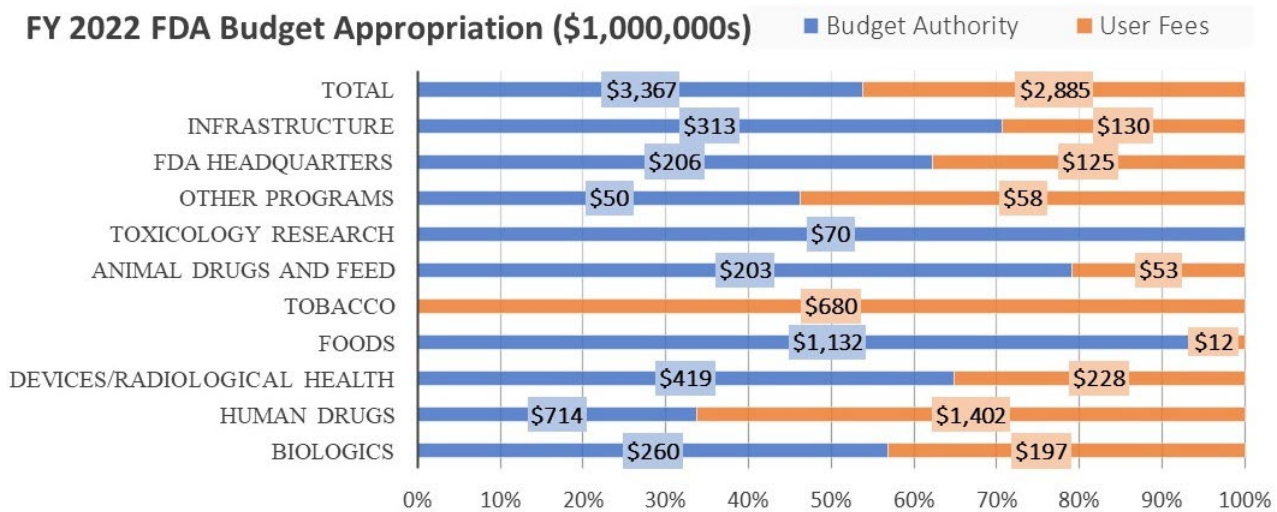
⁸ Over-the-Counter Monograph User Fee Act “OMUFA” passed as part of the 2020 Coronavirus Aid, Relief, and Economic Security Act or “CARES Act”. <https://www.fda.gov/industry/fda-user-fee-programs/over-counter-monograph-drug-user-fee-program-omufa>

⁹ Animal Drug User Fee Act “ADUFA” began in 2003. <https://www.fda.gov/industry/fda-user-fee-programs/animal-drug-user-fee-act-adufa>

¹⁰ Animal Generic Drug User Fee Act “AGDUFA” began in 2008. <https://www.fda.gov/industry/fda-user-fee-programs/animal-generic-drug-user-fee-act-agdufa>

¹¹ The 2009 Family Smoking Prevention and Tobacco Control Act authorized FDA to assess and collect user fees that provide 100% of funding for FDA’s tobacco products and regulatory activities. <https://www.fda.gov/tobacco-products/manufacturing/tobacco-user-fees>

Figure 2. Fiscal Year 2022 FDA Budget Appropriations (\$millions)



Prescription Drug User Fee Act

In 1992, the Prescription Drug User Fee Act (PDUFA) was first enacted, authorizing FDA to assess and collect fees from manufacturers. Since then, a portion of FDA’s budget for the review of drugs and biologics has come from industry user fees. The original goal of PDUFA was to speed the FDA’s application review process for new drugs and biological products without compromising FDA’s standards for new drug safety, efficacy, and quality.¹² Originally, user fees were authorized to support only premarket review activities, which allowed FDA to hire additional staff to help meet its performance goals. Over time, other activities that relate specifically to prescription drug development, such as preclinical drug development, certain post-marketing activities, and enhancements to technology systems, have also been allowed to be paid by user fees.^{4,13,14}

There are two types of PDUFA fees: application fees and program fees. Application fees are one-time fees that are required when an application for a new small molecule drug or biological product is submitted to FDA. The FY2023 application fees are \$3,242,026 per application with clinical data and \$1,621,013 per application for which clinical data is not required.¹⁵ Program fees are annual fees paid by all sponsors of products that are FDA approved and legally marketed. The FY2023 program fees are \$393,933 per sponsor.¹⁵ Waivers or adjustments to user fees are permitted for several reasons, including if a waiver or reduction is necessary to protect the public health, assessment of the user fees would present a significant barrier to innovation due to limited resources or other circumstances, or the applicant involved is a small business submitting its first human drug application for review.

¹² Testimony of Patrizia Cavazzoni and Peter Marks on February 3, 2022 to the House Committee on Energy and Commerce, Subcommittee on Health titled “FDA User Fee Reauthorization: Ensuring Safe and Effective Drugs and Biologics”. <https://www.fda.gov/news-events/congressional-testimony/fda-user-fee-reauthorization-ensuring-safe-and-effective-drugs-and-biologics-02032022>

¹³ Congressional Research Service. (2021). FDA Human Medical Product User Fee Programs (R44750). <https://crsreports.congress.gov/product/details?prodcode=R44750>. Last accessed August 18, 2022.

¹⁴ U.S. Food and Drug Administration. (2022). FY2021 Financial Report to Congress for the Prescription Drug User Fee Act of 1992. <https://www.fda.gov/media/156199/download>. Accessed September 14, 2022.

¹⁵ U.S. Food and Drug Administration. (2022). Prescription Drug User Fee Amendments. <https://www.fda.gov/industry/fda-user-fee-programs/prescription-drug-user-fee-amendments>

Medical Device User Fee Amendments

In 2002, Congress enacted the Medical Device User Fee Modernization Act (MDUFMA) to implement a user fee program for medical devices; MDUFMA is now called the Medical Device User Fee Amendments (MDUFA). The goal of the legislation was to improve the predictability, transparency, and consistency of regulatory processes for medical devices to incentivize innovation and get more products to market faster.¹⁶ For instance, the most recent MDUFA performance goals include agreed-upon timelines for review, process improvements in the pre-marketing and marketing application processes, improved engagement and communication with industry, improvements in scientific and regulatory review capacity, enhanced patient engagement and patient input in the regulatory process, and support for adoption of emerging diagnostics, regular progress reports, and conduct of an independent assessment of the review of device applications.¹⁷

There are two types of user fees for medical device companies. Device manufacturers pay establishment registration fees to FDA when they register their establishments, and they pay application fees when they submit a medical device marketing application for review. User fees are also paid for other submissions, such as annual reports and 513(g) information requests (a request for the agency's views about the classification and the regulatory requirements that may be applicable to a particular device). Generally, establishments that are required to register are also required to list the devices that are made in each registered establishment.¹⁸ All establishments must pay the establishment registration fee (\$6,493 per establishment for FY2023); there are no waivers or reductions for small establishments. The application fee differs by the type of submission, ranging from \$5,961 for a 513(g) information request to \$441,547 for a premarket approval application (PMA) in FY2023. Small businesses pay a reduced application fee – the fees range from \$2,980 to \$110,387—and they can apply for a waiver for their first marketing application.¹⁹

In recent years, FDA has seen unprecedented growth in the number of requests for pre-submission consultations.²⁰ MDUFA IV authorized resources for about 2,350 pre-submissions each year, but the number of pre-submissions over fiscal years 2017-2021 exceeded the anticipated level by up to 1,000 pre-submissions per year (Figure 3).¹⁶

¹⁶ Testimony by Jeffrey Shuren on March 31, 2022 titled “FDA User Fee Reauthorization: Ensuring Safe and Effective Medical Devices”. <https://www.fda.gov/news-events/congressional-testimony/fda-user-fee-reauthorization-ensuring-safe-and-effective-medical-devices-04012022>

¹⁷ U.S. Food and Drug Administration. (2023). Medical Device User Fee Amendments 2022 (MDUFA V).

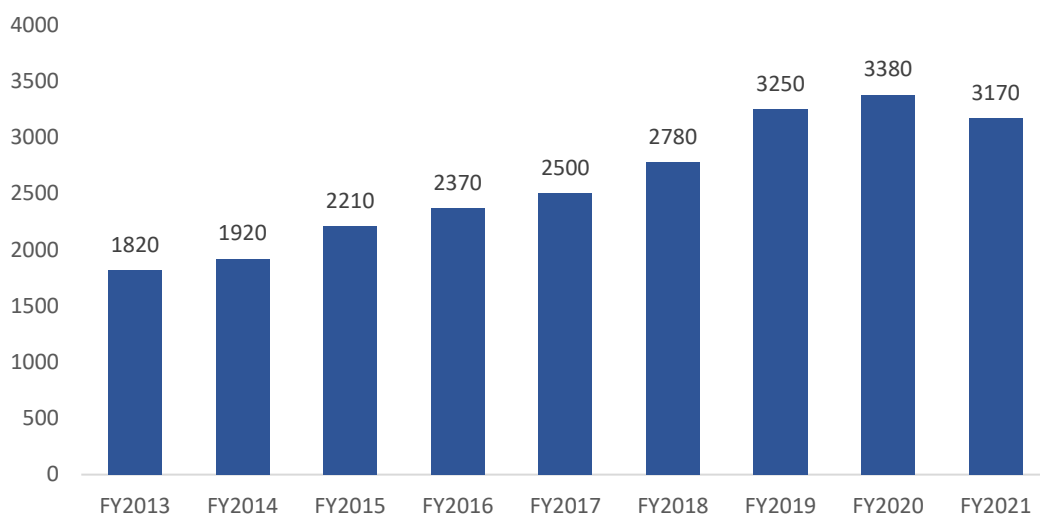
<https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/medical-device-user-fee-amendments-2022-mdufa-v>

¹⁸ U.S. Food and Drug Administration. (2021). Device Registration and Listing. <https://www.fda.gov/medical-devices/how-study-and-market-your-device/device-registration-and-listing>

¹⁹ U.S. Food and Drug Administration. (2022). Medical Device User Fee Amendments (MDUFA). <https://www.fda.gov/industry/fda-user-fee-programs/medical-device-user-fee-amendments-mdufa>

²⁰ Pre-submissions follow a structured process for interactions between FDA and industry. These interactions are intended to obtain FDA feedback on future applications prior to their submission.

Figure 3. Requests for Device Pre-Submission Consultations Received by FDA^{16,21}



Generic Drug User Fee Amendments (GDUFA)

In the years preceding user fees for generic drugs, the number of generic drug applications and the number of foreign facilities making generic drugs grew to such an extent that FDA experienced a backlog of marketing applications. This was a result of lack of resources to keep pace with the growth in the industry.^{22,23} After negotiation and consultation with stakeholders, FDA and the generic drug industry developed a proposal for a user fee program for generic drugs and submitted it to Congress. In 2012, the Generic Drug User Fee Amendments (GDUFA)²⁴ were passed as part of the Food and Drug Administration Safety and Innovation Act (FDASIA), which allowed FDA to assess and collect user fees from drug companies that submit marketing applications for certain generic human drug applications, drug master files holders, and facilities.

GDUFA I (2012 to 2017) enabled FDA to implement enhancements to expedite the review and approval of human generic drugs. It also brought a risk-based approach to good manufacturing practice inspections with the goal of achieving parity of inspection frequency between domestic and foreign manufacturers. More recent goals include reducing the number of review cycles to approval, supporting the development of complex generic drug products, and improving communications with industry.²⁵ GDUFA includes four types of fees.²⁶ Annual program fees depend on the number of approved generic applications (called abbreviated new drug applications or ANDAs) per company.²⁷ In FY2023, program fees ranged from \$162,056 to \$1,620,556 per company. There are also facility fees which vary depending on the type of facility (i.e., active pharmaceutical ingredients (API),

²¹ The definition of a pre-submission changed over time, so it is not possible to have a longer period of observations. Pre-submissions began to be part of the MDUFA negotiations starting when the data are shown here, hence there is no pre-period data available.

²² Congressional Research Service. (2021). The Generic Drug User Fee Amendments (GDUFA): Background and Reauthorization, R46778. <https://crsreports.congress.gov/product/details?prodcode=R46778>

²³ Testimony by Janet Woodcock on March 2, 2017 before the House Committee on Energy and Commerce, Subcommittee on Health, titled "Generic Drug User Fee Act Reauthorization (GDUFA II)". 115th Cong., 1st session, p. 4.

²⁴ U.S. Food and Drug Administration. (2022). Generic Drug User Fee Amendments. <https://www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments>

²⁵ U.S. Food and Drug Administration. (2022). GDUFA Performance Reports. <https://www.fda.gov/about-fda/user-fee-performance-reports/gdufa-performance-reports>

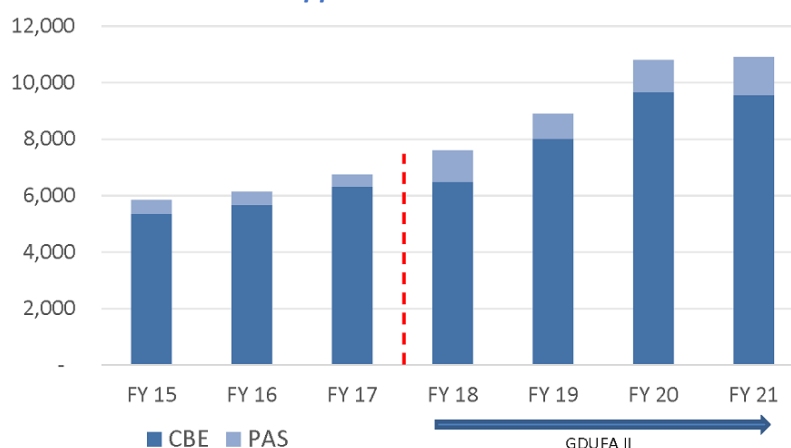
²⁶ In addition to the four categories of fees discussed above, GDUFA also includes a one-time backlog fee for abbreviated new drug applications pending on October 1, 2012 that had not received a tentative approval prior to that date.

²⁷ U.S. Food and Drug Administration. (2022). Generic Drug User Fee Amendments. <https://www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments>

finished dosage form and contract manufacturing organizations) and whether a facility is foreign or domestic. For example, in FY2023 the user fee for an API facility was \$37,544 and \$52,544 per domestic and foreign facility, respectively. There are also fees for manufacturers involved in producing certain types of APIs (called type II active pharmaceutical ingredient drug master file holders) (\$78,293 in FY2023) and for filing an ANDA for FDA review (\$240,582 for FY2023).

Once a generic drug application has been approved by FDA, any changes must be reported to FDA. One of the goals of GDUFA was to reduce the review time of these change requests. Prior-approval supplements (PAS) are required for any major change that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product as these factors may relate to the safety or effectiveness of the drug product; a moderate change requires a “changes being effected” (CBE) notification. The number of PAS and CBE submissions has almost doubled since GDUFA was first passed (Figure 4).²⁴

Figure 4. Generic Drug Applications for Prior-Approval Supplements (PAS) and Changes Being Effected (CBE) Supplement²⁴



Notes: The dashed red line represents passage of GDUFA II. “PAS” is an abbreviation for “prior-approval supplements”, which are required by FDA for applicant holders to submit prior to making any major change to a generic drug. “CBE” is an abbreviation for “changes being effected” supplements, which are required by FDA for applicant holders to submit when making moderate changes to a generic drug.

EVIDENCE ON USER FEES

ASPE conducted literature reviews, including ASPE-generated research and academic research, to identify empirical studies on several topics: the role of user fees on drug prices, the share of the costs for medical product development spent on user fees, and the impact of user fees on review timelines.

Relationship between User Fees and Drug Pricing

In 2021, gross prescription drug spending in the United States was \$603 billion,²⁸ while FDA collected \$1.153 billion in prescription drug user fees.²⁹ This means that, in aggregate, user fees made up 0.20 percent of realized revenue for prescription drugs in 2021. Similarly, for medical devices, the most recent spending

²⁸ Parasrampur, S. & Murphy, S. Trends in Prescription Drug Spending, 2016-2021. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. September 2022.

<https://aspe.hhs.gov/sites/default/files/documents/88c547c976e915fc31fe2c6903ac0bc9/sdp-trends-prescription-drug-spending.pdf>

²⁹ U.S. Food and Drug Administration. FY 2021 Financial Report to Congress for the Prescription Drug User Fee Act of 1992.

<https://www.fda.gov/media/156199/download>

estimates are from 2019, when spending on medical devices was \$199.1 billion.³⁰ In 2019, FDA’s collection of medical device user fees equaled \$208 million, or 0.1 percent of the revenue for medical devices. While these numbers are aggregates, it suggests that the market for medical products remains large and that user fees make up a small portion of the expected revenues (well under 1 percent in both drug and medical device markets). This, in turn, likely means that user fees are not commonly a driving factor when making decisions about bringing products to market or the pricing of products.

We did not find any papers linking user fees to high prices of brand drugs. We identified two studies related to generic drug user fees that could indirectly shed light on this issue via changes in market concentration or market exit, but neither study provides direct quantitative evidence to support the relationship between user fees and drug prices generally or for brand name or generic drugs.^{31,32} Berndt et al. (2018) assessed the structure of the GDUFA I and concluded that it created barriers to entry for new generic drug manufacturers. Dong et al. (2017) found that GDUFA I disproportionately burdened small and new firms and that it favored large firms. This study also suggested that high market concentration and dependence on foreign-supply sources can increase the vulnerability of the supply chain and potentially lead to product shortages and price changes.³³ Neither of these studies directly examined drug prices, and they examined a user fee structure that was replaced by GDUFA II to ameliorate some of the concerns raised by these studies.

User Fees as a Share of the Total Cost of Development

ASPE has completed several research projects that examined the cost of development for different types of medical products. The research examined the cost of development for new drugs, generic drugs, complex medical devices, and vaccines. One of the primary goals in each of these analyses was to examine drivers and barriers to medical product development, including the contribution of FDA user fees to the cost of development.

³⁰ Donahue, G.F. (2021) Estimates of Medical Device Spending in the United States. Report for Advanced Medical Technology Association. <https://www.advamed.org/wp-content/uploads/2021/12/Estimates-Medical-Device-Spending-United-States-Report-2021.pdf>

³¹ Berndt, E. R., Conti, R. M., & Murphy, S. J. (2018). The Generic Drug User Fee Amendments: An Economic Perspective. *Journal of Law and the Biosciences*, 5(1), 103-141.

³² Dong, K., Boehm, G., & Zheng, Q. (2017). Economic Impacts of the Generic Drug User Fee Act Fee Structure. *Value in Health*, 20(6), 792-798.

³³ Lund, S., Manyika, J., Woetzel, J., Barriball, E., Krishnan, M., et al. Risk, Resilience, and Rebalancing in Global Value Chains. McKinsey Global Institute, August 2020.

ASPE developed an analytical model of medical product development using data from public and proprietary sources with coverage from 2000 to 2018. The model estimated the cost, duration, and phase transition success probability associated with each stage of development, including FDA review and approval. The results of the analytical model provided an estimate of the cost of medical product development at each stage of the process from the nonclinical stage to post-marketing. In this model, the cost of the FDA review stage was estimated using user fees paid by industry and the average time it takes for FDA to review a marketing application. The duration of product development varied across medical products, with some drugs taking up to 10 years to develop, and other drugs not reaching the marketing authorization stage. These estimates considered the time it takes to develop a medical product (i.e., “development costs”) and the likelihood that each product was successful at each stage of the development process. That is, these costs included the cost of investment and the cost of failures also known as “capitalized costs.” Our results show that FDA user fees made up approximately 1.0 percent of the total capitalized cost of development for drugs,³⁴ 2.0 percent of the total capitalized cost of development for preventive vaccines, and 0.5 percent of the total capitalized cost of development for complex medical devices.^{35,36}

User fees made up less than 2.0 percent of the total capitalized cost of development for drugs, complex medical devices and preventive vaccines.

In a related report from 2022,³⁷ ASPE developed an analytical framework that examined the expected profit for a generic drug developer in different size drug markets. The framework included characteristics of the type of drugs, the opportunity cost of capital, the fifteen stages of generic drug development, and future revenue expectations. This framework formed the basis for an operational model that can simulate expected changes in the cost of developing a generic drug based on different policy changes, such as a change in user fees.³⁸ This analysis found that the average cost to develop a generic drug was \$2.4 million (\$3.2 million in 2022 dollars) and that it required just under 5 years to bring a generic drug to market. The average capitalized cost was \$5.3 million (\$7.06 in 2022 dollars). FDA user fees to submit an ANDA constituted 1.7 percent (range: 0.2 to 7.0 percent) of expected capitalized costs.

The analysis also assessed the impact of a hypothetical 50 percent decrease in ANDA submission fees. A 50 percent decrease in ANDA submission fees would result in a 1.2 percent (range: 0.1 to 4.8 percent) decrease in expected capitalized costs.³⁹ In contrast, other factors would have a much larger impact on reducing the cost

³⁴ In our model, drugs include biologics except preventive vaccines which are modeled separately.

³⁵ Sertkaya, A., DeVries, R., Jessup, A., Beleche, T. (2022) Estimated Cost of Developing a Therapeutic Complex Medical Device in the US. *JAMA Network Open*, 5(9): e2231609. Doi: 10.1001/jamanetworkopen.2022.31609.

³⁶ Therapeutic complex medical devices are defined as a Class III device that usually sustains or supports life, is implanted, or presents potential unreasonable risk of illness or injury and requires a PMA application to obtain marketing approval in the U.S. These types of applications make up less than 1 percent of all medical device submission and, as such, the results cannot be generalized to other medical devices. Further, there is variability in terms of complexity of medical products, which can result in a large degree of variability around the average development cost.

³⁷ Sertkaya, A., Lord, A., & Berger, C. (2022). Cost of Generic Drug Development and Approval. Report for the Office of the Assistant Secretary for Planning and Evaluation, U.S., Department of Health and Human Services. <https://aspe.hhs.gov/reports/cost-generic-drugs>

³⁸ Broadly speaking, these stages captured the initial R&D phases, in vivo testing, bridging studies, patent challenge and litigation, and FDA review. See Sertkaya et al (2022) for additional details.

³⁹ The hypothetical model assumes that the fee decreases would not affect FDA’s capacity to review applications in a timely manner. Sertkaya et al (2022) note that “a fee decrease of that magnitude could severely hamper FDA’s ability to meet its congressionally mandated review timelines and would likely increase the average FDA ANDA review time estimated in the model. This could potentially counteract the cost-saving effect of FDA ANDA review fee reductions to the generic drug applicant and can even result in an increase in the overall expected capitalized development cost.”

of generic drug development, such as increasing the rate of FDA first-cycle approvals, expanding the use of biowaivers in lieu of bioequivalence studies where possible, removing the incentive for reference product sponsors to “product hop,”⁴⁰ and reforming payment incentives, such as ensuring that generic drugs are placed on preferred formulary tiers.

Taken together, ASPE research suggests that user fees are a small contributor towards the capitalized cost of medical product development, on the order of 0.5 to 2 percent.

Impact of User Fees on FDA Review of Applications

Several studies have assessed the impact of funding on review times. Carpenter et al. (2003) examined whether the source of funding influenced review times with a goal of addressing concerns about pharmaceutical industry influence in the review process.⁴¹ The authors found that user fees shortened New Drug Application (NDA) review times by 3.3 months for every 100 additional staff and concluded that the amount of funding for FDA staff was more influential in shortening NDA review time than the source of funding.⁴¹ Kaitin (1997) also found that NDA review times were shortened after PDUFA, but that user fees did not affect the overall timeline to conduct clinical studies and hence also did not largely affect the overall timeline to bring a medical product to market.⁴² Darrow et al. (2020) found that PDUFA fees increased from \$66 million (\$115 million in 2022 dollars) over the period of 1993-1997 to \$820 million (\$935 million in 2022 dollars) in 2013-2017 and estimated that in 2018 user fees accounted for approximately 80 percent of the salaries of drug application reviewers.⁴³ This same study estimated that FDA review times declined from more than 3 years in 1983 to less than 1 year in 2017, and that FDA accepted more surrogate endpoints and less data in their applications.⁴³ As a result, the authors estimated that legislation from 1983 to 2018, including user fees, increased the number of new drug approvals. The mean annual number of new drug approvals, including biologics, increased from 34 in 1990-1999 to 41 in 2010-2018.⁴³ The median annual number of generic drugs approved increased from 284 prior to GDUFA to 588 between 2013 and 2018.⁴³ More recent data show that in fiscal year 2021, FDA approved 579 ANDAs and tentatively approved 157 ANDAs.⁴⁴ An older study conducted by Berndt et al. (2004) estimated that approximately two-thirds of the decline in approval times can be attributed to PDUFA.⁴⁵ A study by Mitchell et al. (2022) concluded that the PDUFA model supported the implementation of a range of changes to FDA policy and statutory changes that included promoting the expedited review programs (e.g. priority review and the breakthrough and fast track designation); increased opportunities for industry meetings with FDA about clinical trial design; guidance on rules regarding industry dissemination of peer reviewed scientific literature and other health care economic information to providers; and incentives to encourage market entry of new generic drugs. The authors suggest that FDA’s budgetary dependence on user fees and industry’s required participation in PDUFA negotiations may advantage the industry.⁴⁶

⁴⁰ A “product hop” refers to a practice where a brand company attempts to preserve its market dominance by creating a new version of a product with incremental innovation that is protected by a longer-term patent.

⁴¹ Carpenter, D., Chernew, M., Smith, D. G., & Fendrick, A. M. (2003). Approval Times for New Drugs: Does The Source Of Funding For FDA Staff Matter? The Amount of Resources Devoted to FDA Review, Not the Source of Funding, Was Likely the Principal Driver Behind Shrinking Approval Times Since 1980. *Health Affairs*, 22(Suppl1), W3-618.

⁴² Kaitin, K. I. (1997). The Prescription Drug User Fee Act of 1992 and the New Drug Development Process. *American Journal of Therapeutics*, 4(5-6), 167-172.

⁴³ Darrow, J. J., Avorn, J., & Kesselheim, A. S. (2020). FDA Approval and Regulation of Pharmaceuticals, 1983-2018. *JAMA*, 323(2), 164-176.

⁴⁴ U.S. Food and Drug Administration. FY 2021 Performance Report to Congress for the Generic Drug User Fee Amendments. <https://www.fda.gov/media/155760/download>.

⁴⁵ Berndt, E. R., Gottschalk, A. H., Philipson, T., & Strobeck, M. W. (2005). Assessing the Impacts of the Prescription Drug User Fee Acts (PDUFA) on the FDA Approval Process. *In Forum for Health Economics & Policy* (Vol. 8, No. 1). De Gruyter.

⁴⁶ Mitchell, A. P., Trivedi, N. U., & Bach, P. B. (2022). The Prescription Drug User Fee Act: Much More Than User Fees. *Medical Care*, 60(4), 287-293.

Economic Benefits of User Fees

User fees help support allowable activities that have implications for patient safety and access to new medical products. For example, user fees can support increased staffing and training to speed up review of NDA and Biologics License Applications (BLA) manufacturing supplements. NDA or BLA manufacturing supplements are submitted to FDA when a manufacturer intends to make post-approval changes to manufacturing sites, manufacturing processes, or other changes that are considered a major change.⁴⁷ A major change is one that has a substantial potential to have an adverse effect on the safety and efficacy of the approved product and must be approved by FDA before it is made. Further, additional staffing can help bring medical products to market more expeditiously and thereby increase medical care options for patients.

Putting all of these various effects together, a few studies have examined the impact of medical product user fees, including the economic benefits of user fees. One of the few studies that provides quantitative estimates of the economic benefits of PDUFA on society is a study by Philipson et al. (2008), which found that PDUFA resulted in net benefits for consumers and manufacturers. Specifically, the authors showed that PDUFA raised manufacturers' returns on investment by \$7 to \$11 billion (\$9.3 to \$14.7 billion in 2022 dollars) or about \$25 to \$39 million per drug launched (\$33.3 to \$52.0 million in 2022 dollars).⁴⁸ These benefits were mainly driven by reduced review times, which accelerated the launch of new drugs to market and hence to patients. These estimates suggest that for \$1 paid in user fees, the return for manufacturers is between \$8.60 and \$13 (\$11.5 and \$17.3 million in 2022 dollars). Philipson et al. (2008) also showed that consumer welfare as measured by the health benefits from access to more rapid approval of drugs under PDUFA increased between \$7 billion and \$20 billion (\$9.3 and \$26.6 billion in 2022 dollars).⁴⁸ These estimated benefits are substantial in comparison to user fees (about \$3 million per NDA submission or \$1.8 billion in total user fees for devices, human drugs and biologics authorized in FY2022). Further, these estimates can also be translated into 140,000 to 310,000 life years saved from patients who have more rapid access of drugs.⁴⁸ The authors concluded that the estimated net benefits far outweighed the estimated 56,000 life years lost due to adverse events related to the use of approved drugs that were subject to PDUFA fees and later withdrawn for safety reasons.⁴⁸ It is important to note that this paper was published 15 years ago and there have been significant changes in the prescription drug marketplace and landscape in the intervening period, so further examination of whether these estimates still hold would be beneficial.

Discussion and Conclusion

The existing body of work points to benefits to consumers and industry from user fees in the form of increased access to new medical products, faster review timelines, and improvements in the transparency of the regulatory review process. The evidence also suggests that these benefits outweigh the costs, as user fees represent a small percent of development costs and serve as a crucial source of funding for regulatory activities and approval of medical products. User fees account for 66 percent of the human drugs budget, 43 percent of the biologics budget, and 35 percent of the medical devices budget.

Most of the existing research on user fees has focused on the largest user fee programs for prescription drugs and generics; however, examining the impact of user fees for biosimilars and medical devices may provide new insights. This is particularly important in light of the COVID-19 pandemic during which there has been an

⁴⁷ FDA's regulations also require submission of a supplement for certain other than major changes. For example, a supplement submission is required at least 30 days prior to distribution of the product made using the change.

⁴⁸ Philipson, T., Berndt, E. R., Gottschalk, A. H., & Sun, E. (2008). Cost-benefit Analysis of the FDA: The Case of the Prescription Drug User Fee Acts. *Journal of Public Economics*, 92(5-6), 1306-1325

unprecedented increase in the number of medical device submissions to FDA. As the pace of technological development continues to increase, new medical products will continue evolving and become more complex. This in turn requires having adequate funding and resources to conduct regulatory activities and reviews necessary to keep pace. However, given that some of the key studies are 20 years old, there could be potential value in updating the research on user fees in recognition of the changing marketplace and landscape.

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