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FDA Human Medical Product User Fee Programs: In Brief

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Contents

Overview 1
User Fees and the FDA Budget 3
Medical Product User Fee Programs 4
PDUFA 4
MDUFA 5
GDUFA 7
BsUFA 8

Figures

Figure B-1. FDA Human Medical Product User Fee Programs: Total Costs, by Funding Source 11

Tables

Table A-1. FDA Human Medical Product User Fee Programs 10

Appendixes

Appendix A. FDA Human Medical Product User Fee Programs 10
Appendix B. User Fees and Appropriations 11
Appendix C. Selected CRS Products Related to FDA Regulation of Human Medical Products 12

Contacts

Author Information 12

Overview

The Food and Drug Administration (FDA) regulates human medical products to ensure they are safe and effective for their intended use in patients.[1] Medical products include prescription and nonprescription (over-the-counter) drugs, biologics, and medical devices. FDA regulation of these products involves both premarket and postmarket regulatory requirements.[2] Premarket requirements, which use a significant portion of the agency's resources, include the review of products and product applications for FDA approval, authorization, or clearance prior to marketing. Postmarket requirements are varied, but may include passive surveillance mechanisms used to monitor the performance of medical products once they are marketed and certain postmarket studies and reporting.

FDA Review of Human Medical Products

Center for Biologics Evaluation and Research (CBER) regulates traditional biologics, such as vaccines.

Center for Devices and Radiological Health (CDRH) regulates medical devices.

Center for Drug Evaluation and Research (CDER) regulates prescription brand-name and generic drugs, over-the-counter drugs, and most therapeutic biologics.

To support these premarket and postmarket activities, the agency relies on (1) discretionary appropriations provided through the annual appropriations process, and (2) user fees paid by each regulated industry. The primary purpose of the user fee programs is to reduce the time necessary to review and make decisions on medical product marketing applications. Lengthy review times affect the industry, which waits to market its products, and patients, who wait to use these products. Some critics of the current scope of the user fee programs are concerned that FDA's mission to protect public health may be compromised if reliance on these fees affects the impartiality of FDA's scientists.

Certain user fee programs are reauthorized together in legislation on a five-year cycle, with authority for the actual collection and expenditure of the fees provided each year through the annual appropriations process.[3] These programs include those for prescription drugs, medical devices, generic drugs, and biosimilars.[4] The original authorizing legislation for each of these four user fee programs is as follows: (1) the Prescription Drug User Fee Act of 1992 (PDUFA, P.L. 102-571); (2) the Medical Device User Fee and Modernization Act of 2002 (MDUFMA, P.L. 107-250); (3) the Generic Drug User Fee Amendments of 2012 (GDUFA, Title III of the Food and Drug Administration Safety and Innovation Act [FDASIA], P.L. 112-144); and (4) the Biosimilar User Fee Act of 2012 (BsUFA, Title IV of FDASIA, P.L. 112-144). **Appendix A** outlines various features of these four user fee programs, and **Appendix C** lists relevant CRS reports related to medical product regulation.

[1] FDA also regulates animal drugs and feeds, human foods, dietary supplements, cosmetics, radiological devices, and tobacco products.

[2] For more information, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*.

[3] For a detailed discussion of the funding sources for the review human medical products, see CRS Report R44582, *Overview of Funding Mechanisms in the Federal Budget Process, and Selected Examples*.

[4] The FDA also has user fee authorities for over the counter monograph drugs, animal drugs, tobacco products, priority review vouchers, food reinspection, food recall, voluntary qualified food importer, outsourcing facilities (related to drug compounding), and some wholesale distributors and third-party logistics providers (related to pharmaceutical supply chain security). These other authorities are not addressed in this report.

Due to the importance of user fees to FDA's budget, reauthorization of the user fee programs has been considered to be "must pass" legislation. Congress generally uses the reauthorization bill to address related FDA regulatory concerns; it therefore serves as an important driver for the ongoing modification of overall agency regulatory policy. The Food and Drug Administration Reauthorization Act of 2017 (FDARA,), the most recent user fee legislation enacted in August of 2017, reauthorized each of the four human medical product user fee programs for five more years, from FY2018 through FY2022. FDARA (P.L. 115-52) consists of nine titles; the first four authorize FDA to collect fees and use the revenue to support specified activities for the review of prescription brand-name drugs and biological products, medical devices, generic drugs, and biosimilar biological products. FDARA Titles V through IX addressed a range of other policy issues including pediatric drugs and devices, reauthorizations and improvements related to drugs, device inspection and regulatory improvements, generic drug access, and a set of miscellaneous provisions. However, the 21st Century Cures Act (Division A, P.L. 114-255), enacted just prior to FDARA in December of 2016, included numerous provisions that modified drug and device regulation, perhaps reducing the number of such provisions that were added to FDARA (P.L. 115-52).

A shared element of all four user fee programs is that the user fees are to supplement congressional appropriations, not replace them. The authorizing laws include limiting conditions, known as "triggers," to enforce this goal. FDA may collect and use fees only if the direct appropriations for specified activities involved in the review of products remains at a level at least equal (adjusted for inflation) to an amount or benchmark specified in each law.[5] Originally, the fees were authorized to be used to support only premarket review activities, allowing FDA to hire additional staff to review premarket applications with the goal of reducing review time. Over time, the scope of allowable activities that may be paid for with user fee revenue has been expanded to include, for example, FDA support of manufacturers' preclinical drug development and certain postmarket activities.

In exchange for paying user fees, industry receives from FDA a commitment to meet certain performance goals, such as completing premarket review within a specified timeframe. Prior to each five-year reauthorization cycle, FDA and industry negotiate the performance goals, which are finalized in a written agreement. The reauthorization process allows for input from other relevant stakeholders, including academic experts and representatives of patient and consumer advocacy groups, and provides opportunity for public comment on the agreement. For the next reauthorization cycle, the Federal Food, Drug, and Cosmetic Act (FFDCA) requires the Health and Human Services (HHS) Secretary to submit the four user fee agreements to Congress by January 15, 2022.[6] In each previous reauthorization, Congress has accepted unchanged the terms and conditions as negotiated between FDA and the industry. The four performance goal documents for FY2018 through FY2022 are provided on the FDA website.[7]

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[5] Prescription drugs, FFDCA §736(f) and (g); medical devices, FFDCA §738(h); generic drugs, FFDCA §744B(h) and (i); biosimilars, FFDCA §744H(f). Further details on each of these legal conditions are available in the FDA user fee financial reports: http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/default.htm.

[6] Prescription drugs, FFDCA §736B(f)(5); medical devices, FFDCA §738A(b)(5); generic drugs, FFDCA §744C(f)(5); biosimilars, FFDCA §744I(f)(3).

[7] PDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf;
GDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf and http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525236.pdf;
MDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526395.pdf and http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526532.pdf;

User Fees and the FDA Budget

FDA's budget has two funding streams: annual appropriations (i.e., discretionary budget authority, or BA) and industry user fees.[8] In FDA's annual appropriation, Congress sets both the total amount of appropriated funds and the amount of user fees that the agency is authorized to collect and obligate for that fiscal year. Since the enactment of PDUFA in 1992, FDA's spending from user fees has generally increased, both in absolute terms and as a share of FDA's total budget, accounting for over 40% of the agency's FY2019 total program level.[9] **Appendix B** provides information on the relative proportion of costs supported by user fee revenue and appropriations for each of the four user fee programs. The following paragraphs look at the funding for each of the four human medical product user fee programs individually.

Prescription drug user fees were first collected in FY1993 and have comprised an increasing proportion of the FDA's budget that is focused on prescription drug regulation. In FY2007, prescription drug user fees provided 56% of the PDUFA program total costs (appropriations provided 44%); in FY2019 (from the most recent financial report available), user fees covered 71% of PDUFA program total costs (appropriations covered 29%).[10] While most of PDUFA revenue supports activities managed by Center for Drug Evaluation and Research (CDER), PDUFA revenue also contributes to other FDA organizational components that support the PDUFA program, including Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), the Office of Regulatory Affairs (ORA), and FDA headquarters.[11]

Medical device user fees were first collected in FY2003 and have comprised an increasing proportion of FDA's budget that is focused on device regulation. In FY2007, medical device user fees accounted for 17% of the MDUFA program total costs, compared with 30% in FY2019.[12] While most of MDUFA revenue supports activities managed by CDRH, MDUFA revenue also contributes to other parts of FDA that support the MDUFA program including CBER, ORA, and FDA headquarters.[13]

In FY2013, the first year generic drug user fees were collected, user fees accounted for 45% of the GDUFA program total costs compared with 72% in FY2019.[14] While most of GDUFA fee revenue supports activities managed by CDER, GDUFA revenue also contributes to other FDA components that support the GDUFA program, including CBER, ORA, and FDA headquarters.[15]

BsUFA: http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/default.htm. The summary document for MDUFA contains statutory language, and the summary document for GDUFA contains the new fee structure.

[8] For more information about the FDA budget generally, and a discussion of user fees within the budget, see CRS Report R44576, *The Food and Drug Administration (FDA) Budget: Fact Sheet*.

[9] CRS Report R44576, *The Food and Drug Administration (FDA) Budget: Fact Sheet*.

[10] FDA, *FY2019 PDUFA Financial Report*, Table 8: Historical Prescription Drug User Fee Obligations by Funding Source As of September 30 of Each Fiscal Year, p. 17, at https://www.fda.gov/media/138424/download.

[11] FDA, *FY2019 PDUFA Financial Report*, Table 9: Historical Trend of Total Process FTEs Utilized by Organization as of September 30 of Each Fiscal Year, p. 18.

[12] FDA, *FY2019 MDUFA Financial Report*, Table 8: Historical Trend of MDUFA Program Costs by Funding Source as of September 30 of Each Fiscal Year, p. 15, at https://www.fda.gov/media/136034/download.

[13] FDA, *FY2019 MDUFA Financial Report*, Table 9: Historical Trend of Medical Device User Fee Total Process FTEs Utilized by Organization as of September 30 of Each Fiscal Year, p. 15.

[14] FDA, *FY2019 GDUFA Financial Report*, Table 8: Historical Generic Drug User Fee Obligations by Funding Source as of September 30 of Each Fiscal Year, p. 16, at https://www.fda.gov/media/139343/download.

[15] FDA, *FY2019 GDUFA Financial Report*, Table 9: Historical Trend of Total FTEs Utilized by Organization as of

In FY2013, the first year biosimilar user fees were collected, user fees accounted for 0% of the BsUFA program total costs compared with 64% in FY2019.[16] While most of BsUFA revenue supports activities managed by CDER, BsUFA revenue also contributes to other parts of FDA that support the BsUFA program, including CBER, ORA, and FDA headquarters.[17]

Medical Product User Fee Programs

PDUFA

Prior to marketing, a manufacturer must submit a new drug application (NDA) or a biologics license application (BLA) to FDA, demonstrating a drug or biologic's safety and effectiveness.[18] FDA scientific and regulatory personnel review the NDA or BLA and prepare written assessments in several categories—medical, chemistry, statistical, pharmacology, clinical pharmacology and biopharmaceutics, risk assessment and risk mitigation, proprietary name, patient labeling—and then decide whether or not to approve the drug or biologic.[19]

In 1992, PDUFA (later called PDUFA I) gave FDA the authority to collect fees from the pharmaceutical industry and use the revenue to support "the process for the review of human drug applications."[20] That five-year authority, which covered both NDAs and BLAs, has been renewed on five subsequent occasions, by PDUFA II (1997), PDUFA III (2002), PDUFA IV (2007), PDUFA V (2012), and PDUFA VI (2017). PDUFA I authorized FDA to use the fee revenue to fund the "process for the review of human drug applications" and defined what that process encompassed. Congress has amended that definition to expand the scope of activities covered by PDUFA. PDUFA I covered activities that fit within the time window from when a manufacturer submits an NDA or a BLA until FDA makes its decision on that application, (e.g., review of applications, letters from FDA to applicants outlining deficiencies in their applications, and facility inspections). With subsequent amendments made by PDUFA II, III, and IV, FDA may now use PDUFA fees for activities during a drug's preclinical development, clinical trials, and postapproval marketing periods, including postmarket safety activities such as adverse-event data-collection systems, and requirements relating to postapproval studies, labeling changes, and risk evaluation and mitigation strategies.

Each five-year authorization sets a total amount of fee revenue for the first year and provides a formula for annual adjustments to that total based on inflation and workload changes. PDUFA VI set an annual base revenue of $878.6 million for FY2018, to be adjusted as specified.[21] It also

September 30 of Each Fiscal Year, p. 16.

[16] FDA, *FY2019 BsUFA Financial Report*, Table 8: Historical Biosimilar Biological Product User Fee Obligations by Funding Source as of September 30 of Each Fiscal Year, p. 16, at https://www.fda.gov/media/139342/download.

[17] FDA, *FY2019 BsUFA Financial Report*, Table 9: Historical Trend of Total Process FTEs Utilized by Organization as of September 30 of Each Fiscal Year, p. 16.

[18] For purposes of PDUFA, the term *prescription drug* includes both small molecule, chemical drugs approved under Section 505 of the FFDCA, as well as biologics (drugs derived from or made in living organisms) licensed under Section 351 of the Public Health Service Act (PHSA).

[19] The listed categories are the sections of drug approval packages posted by FDA; for example, see the November 2016 files regarding Sanofi's Soliqua 100/33 (insulin glargine and lixisenatide), http://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/208673Orig1_toc.cfm.

[20] P.L. 102-571.

[21] FFDCA §736(b) & (c). See CRS Report R44864, *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI* for details of the various adjustments.

modified the inflation adjustment; replaced the workload adjustment with a capacity planning adjuster; eliminated the final year adjustment provisions and established an annual operating reserve adjustment; added an additional direct cost adjustment; and specified additional dollar amounts for each year.[22]

PDUFA I through V had required that three types of fees each contribute one-third of the fee revenue every year: an application fee, an annual establishment fee, and an annual product fee.[23] PDUFA VI established a new user fee structure, eliminating the product and establishment fees, and adding a *program fee*.[24] It continued the *application fee*, while eliminating the fee for a supplemental application. PDUFA VI requires that user fees be waived or reduced under certain circumstances (e.g., if necessary to protect the public health or if the applicant is a small business submitting its first human drug application). Under the new law, 80% of the total prescription drug user fee revenue comes from program fees and 20% from application fees.[25]

PDUFA Fee Types

Application fee: The sponsor of the application (usually the drug manufacturer) must pay a fee each time it submits an NDA or a BLA for FDA review.

Program fee: The sponsor must pay an annual program fee for each prescription drug product that is identified in an approved application.

MDUFA

Medical devices are used to diagnose, treat, monitor, or prevent a disease or condition in a patient. FDA describes medical devices as ranging "from simple tongue depressors and bedpans to complex programmable pacemakers, and closed loop artificial pancreas systems."[26] FDA classifies devices based on their risk to the patient: low-risk devices are class I, moderate-risk are class II, and high-risk are class III. Given the breadth of devices on the market and the different risks they may pose to the consumer, only certain devices are required to undergo premarket review to provide reasonable assurance of safety and effectiveness. The three most common pathways for premarket review of a device include (1) premarket notification (510(k)), (2) premarket approval (PMA), and (3) De Novo marketing authorization. A device's regulatory class generally dictates the applicable premarket review pathway.

Most class I and some class II devices are exempt from premarket review altogether. The remaining class I and class II devices are subject to premarket notification, also known as a 510(k) *clearance*. To receive a 510(k) *clearance*, a manufacturer must submit certain materials to FDA at least 90 days prior to marketing, demonstrating that the device proposed to be marketed is

[22] See *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI* for details of the various adjustments.

[23] Each manufacturer was required to pay an annual *establishment fee* for each of its manufacturing establishments, an annual *product fee* for each product that fits within PDUFA's definition, and an *application fee*.

[24] PDUFA VI adds the limitation that a person named as the applicant in an approved application cannot be assessed more than five program fees in a fiscal year for prescription drug products identified in such approved application.

[25] FFDCA §736(b)(2).

[26] FDA, Medical Devices, "Is the Product a Medical Device," at http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/classifyyourdevice/ucm051512.htm.

substantially equivalent to a device already on the market. As of September 30, 2020, 87% of 510(k)s accepted for review in FY2020 were determined to be substantially equivalent.[27]

Class III devices are subject to a premarket approval (PMA) application that includes evidence providing reasonable assurance that the device is safe and effective. A successful PMA results in device *approval*. As of September 30, 2020, 83% of PMAs accepted for filing in FY2020 were approved by FDA.[28]

New devices—that is, devices that were not on the market when the Medical Device Amendments of 1976 (MDA; P.L. 94-295) were enacted—are automatically placed into class III, regardless of the risk posed to the consumer. The De Novo pathway allows for the reclassification of new, low or moderate risk devices into class I or II. Devices that are reviewed through this pathway are granted *marketing authorization*. As of September 30, 2020, 50% of De Novos accepted for filing in FY2020 were granted marketing authorization.[29]

Congress gave FDA the authority to collect user fees from the medical device industry in 2002 and renewed that authority three times: MDUFA II (2007), MDUFA III (2012), and MDUFA IV (2017). As noted, class I and some class II medical devices are exempt from premarket review and payment of the associated fee. Small businesses—those with gross receipts below a specified amount—pay reduced premarket review fees and have some fees waived altogether.

In addition to premarket review fees, there are also fees for when a manufacturer requests approval of a significant change in the design or performance of a device approved via the PMA pathway; these are called PMA supplements. The original 2002 user fee law had only authorized FDA to collect fees for premarket review, such as for PMA applications, PMA supplements, or 510(k) notifications. MDUFA II added two types of annual fees in order to generate a more stable revenue stream for the agency: establishment registration fees, paid by most device establishments registered with FDA; and product fees, paid for class III devices for which periodic reporting is required. MDUFA II also added two additional types of application fees[30] and substantially lowered all existing application fee amounts. MDUFA III changed the definition of "establishment subject to a registration fee," increasing the number paying the fee.

Under MDUFA I through III, user fee revenue could be used only for activities associated with premarket review of medical devices. MDUFA IV fees also partially fund postmarket surveillance of medical devices by collecting real-world evidence from different sources (such as registries, electronic health records, and other digital sources) via the National Evaluation System for health Technology (NEST).[31]

MDUFA fee amounts are set as a percentage of the PMA fee, or base fee. The law sets both the base fee amount for each fiscal year, and the percentage of the base fee that constitutes most other fees. MDUFA IV changed the 510(k) fee from 2% of the PMA fee to 3.4% of the PMA fee, added a new fee (De Novo, 30% of the PMA fee), and changed the 510(k) fee paid by small businesses (from 50% of the PMA fee to 25%).[32] The law requires the total revenue amount be adjusted by

[27] MDUFA IV Performance Report, December 15, 2020, p. 117 at https://www.fda.gov/media/144600/download.

[28] MDUFA IV Performance Report, December 15, 2020, p. 24 at https://www.fda.gov/media/144600/download.

[29] MDUFA IV Performance Report, December 15, 2020, p. 179 at https://www.fda.gov/media/144600/download.

[30] The two applications are (1) the 30-Day Notice, used by a manufacturer to request modifications in manufacturing procedures, and (2) the De Novo pathway.

[31] For further information about NEST, see FDA, "National Evaluation System for health Technology (NEST)," https://www.fda.gov/about-fda/cdrh-reports/national-evaluation-system-health-technology-nest.

[32] FFDCA §738(a) & (d). For more information, see CRS Report R44517, *The FDA Medical Device User Fee*

an inflation adjustment; the base fee is increased accordingly to generate the inflation-adjusted total revenue amount.[33] The establishment fee may be increased as necessary so that total fees collected for the fiscal year generates the total adjusted revenue amount.

MDUFA Fee Types

Application fee: The sponsor of a medical device must pay a fee for each submission (e.g., PMA, PMA supplement, a 510(k), De Novo).

Establishment fee: Sponsors whose establishment meets the MDUFA definition must pay an annual registration fee.

Periodic reporting fee: Certain class III device sponsors must pay an annual fee.

GDUFA

Generic drugs are approved under an abbreviated pathway created by the Hatch-Waxman Act.[34] Rather than replicate and submit data from pre-clinical and clinical investigations to prove safety and effectiveness, a generic drug company may submit an abbreviated new drug application (ANDA) relying on FDA's previous findings of safety and effectiveness for the reference drug (typically, a brand-name drug). In the ANDA, the applicant must demonstrate that the generic version is pharmaceutically equivalent (i.e., same active ingredient(s), strength, dosage form, route of administration) and bioequivalent to the reference drug.[35] Because the generic sponsor does not have the expense of product development or animal or human clinical trials, it can offer its product at a lower price than the brand-name sponsor does for its product. An ANDA must include proposed labeling for the generic drug, which must be the same as that for the reference drug, with some exceptions.[36] The ANDA also must provide information about the generic's chemistry, manufacturing and controls to ensure that the manufacturer can make the drug correctly and consistently.[37]

Due to an increase in the number of ANDAs submitted to FDA for review, and an increase in the number of foreign facilities making generic drugs, prior to GDUFA, the agency lacked the resources to keep pace, resulting in a backlog of submitted ANDAs. Generic drug companies submitting ANDAs were not subject to user fees from FDA nor were they included in the scope of activities covered by PDUFA fees.[38]

GDUFA I authorized FDA to collect fees from generic drug companies to supplement the cost of certain human generic drug activities: review of ANDAs and drug master files (DMFs);[39] approval, deficiency, and complete response letters; facility inspections; monitoring or research;

Program: MDUFA IV Reauthorization.

[33] FFDCA §738(b) & (c).

[34] The Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417), often referred to as the Hatch-Waxman Act, amended the FFDCA to allow a generic drug manufacturer to submit an abbreviated NDA (ANDA) to the FDA for premarket review.

[35] FFDCA §505(j)(2) and 21 C.F.R. §314.94.

[36] FFDCA §505(j)(2)(A)(v).

[37] 21 C.F.R. §314.94(a)(9).

[38] For more information, see CRS Report R44703, *Generic Drugs and GDUFA Reauthorization: In Brief*.

[39] A Drug Master File (DMF) is a voluntary submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs. The information contained in the DMF may be used to support an Investigational New Drug Application (IND), an NDA, an ANDA, another DMF, an Export Application, or amendments and supplements to any of these; however, it cannot be used as a substitute for an IND, NDA, ANDA, or export application.

postmarket safety activities; and regulatory science. In exchange, FDA committed to meeting certain performance goals[40] and to taking a "first action" by the end of FY2017 on 90% of the backlog applications that were submitted pre-GDUFA and still pending on October 1, 2012. As of September 30, 2017, FDA had taken action on 98% of the ANDAs in the backlog that were pending review as of October 1, 2012.[41] GDUFA I set a total amount of fee revenue for the first year and provided a formula for annual adjustments to that total based on inflation and workload changes. It established a one-time backlog fee for ANDAs pending as of October 1, 2012.

GDUFA II made modifications to the fee amounts and fee structure to account for increased workload. For example, the total fee revenue amount for the first year of GDUFA II (FY2018) was increased to $493,600,000, to be adjusted annually for inflation.[42] GDUFA II also created a new generic drug applicant program fee, to be paid annually and tiered based on the number of approved ANDAs an applicant owns. It eliminated the prior approval supplement (PAS) fee and provided that fees for foreign generic drug and active pharmaceutical ingredient (API)[43] facilities are $15,000 higher than for domestic facilities.[44] GDUFA II specified the amount to be derived from each fee type: 35% from the new generic drug applicant program fees, 33% from ANDA fees, 5% from DMF fees, 20% from generic drug facilities, and 7% from API facilities.[45] This restructuring was intended to shift the burden toward annual program fees rather than application fees to provide more predictability in revenue.[46] (The volume of applications fluctuates from year to year, whereas the amount of facilities and approved ANDA holders is relatively stable.)

GDUFA Fee Types

Drug Master File fee: The sponsor of a Type II API DMF in a generic drug submission must pay an annual fee for each DMF.

Application fee: The sponsor of an ANDA must pay a fee for each submission.

Facility fee: Generic drug manufacturers must pay an annual fee for each manufacturing establishment.

Program fee: The sponsor of an ANDA must pay an annual fee based on the number of approved ANDAs the sponsor owns.

BsUFA

A biologic is a therapeutic that is made from living organisms.[47] Compared with conventional chemical drugs, biologics are relatively large and complex molecules. A biosimilar is a biologic

[40] FDA, "Generic Drug User Fee Act Program Performance Goals and Procedures," FY2012-FY2017, https://www.fda.gov/media/82022/download.

[41] FDA, "FY2017 Performance Report to Congress for the Generic Drug User Fee Amendments," https://www.fda.gov/media/113302/download.

[42] FFDCA §744B(b) & (c).

[43] An API is defined as a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended to be used as a component of a drug and to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or a substance intended for final crystallization, purification, or salt formation, or any combination of those activities (FFDCA §744A(2)).

[44] FFDCA §744B(b)(2)(C) & (D).

[45] FFDCA §744B(b)(2).

[46] FDA, "GDUFA II Fee Structure Summary," https://www.fda.gov/media/101064/download.

[47] PHSA Section 351(i) defines a biologic as "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a

that is highly similar, but not structurally identical, to the reference product (i.e., the brand-name biologic).[48]

The cost of biologics is often higher than small molecule prescriptions drugs. To bring competition to the biologics market, in 2010, the Biologics Price Competition and Innovation Act (BPCIA) was enacted as Title VII of the Patient Protection and Affordable Care Act (ACA, P.L. 111-148). The BPCIA established an abbreviated pathway under Section 351(k) of the PHSA for licensure of biologics that are demonstrated to be "highly similar" (biosimilar) to or "interchangeable" with an FDA-licensed reference product. A company interested in marketing a biosimilar product in the United States must submit to FDA a BLA that provides information demonstrating, among other things, biosimilarity based on data from analytical studies (structural and functional tests), animal studies (toxicity tests), and a clinical study or studies (tests in human patients). FDA may decide, at its discretion, that a certain study or studies are unnecessary in a biosimilar application.[49]

Authority to collect user fees was provided by the Biosimilar User Fee Act of 2012 (BsUFA I, Title IV of FDASIA, P.L. 112-144) and was reauthorized by title IV of FDARA (BsUFA II). FDA may use BsUFA fees for activities necessary for the review of submissions in connection with biosimilar product development and the review of biosimilar applications.[50] BsUFA II set the total fee revenue amount for FY2018 at $45,000,000 and established that the total revenue amounts for FY2019 through FY2022 are based on a formula that takes into account the annual base revenue for the fiscal year, a new inflation adjustment, a new capacity planning adjustment, and the operating reserve for the fiscal year.[51] BsUFA II removed the establishment fee and replaced it with a new biosimilar biological product program fee, stipulating that product sponsors shall not be assessed more than five biosimilar biological product program fees for a fiscal year per application. BsUFA II removed the supplement application fee and changed the application fee by no longer reducing the application fee by the cumulative amount of previously paid fees for the product. The biosimilar application fee may be waived for the first such application from a small business, defined as an entity, including affiliates, with fewer than 500 employees that does not have an approved drug or biosimilar product introduced into commerce.[52]

BsUFA Fee Types

Initial product development fee: The sponsor of a biosimilar must pay a fee for development meetings with FDA.

Annual product development fee: The sponsor of a biosimilar must also pay an annual fee while the biosimilar is in the development program.

Reactivation fee: A sponsor that discontinues participation in the biosimilar development program must pay a reactivation fee to resume development.

Application fee: The sponsor must pay a fee each time it submits a new biosimilar application.

Program fee: The sponsor of a biosimilar biological product application must pay an annual program fee.

disease or condition of human beings. For more information, see CRS Report R44620, *Biologics and Biosimilars: Background and Key Issues*.

[48] This is in contrast to a generic chemical drug, which is considered an exact copy of a brand-name chemical drug (i.e., the reference drug).

[49] PHSA §351(k)(2)(A).

[50] FFDCA §744G(9) and (13).

[51] FFDCA §744H(b) & (c).

[52] FFDCA §744H(d).

Appendix A. FDA Human Medical Product User Fee Programs

Table A-1. FDA Human Medical Product User Fee Programs

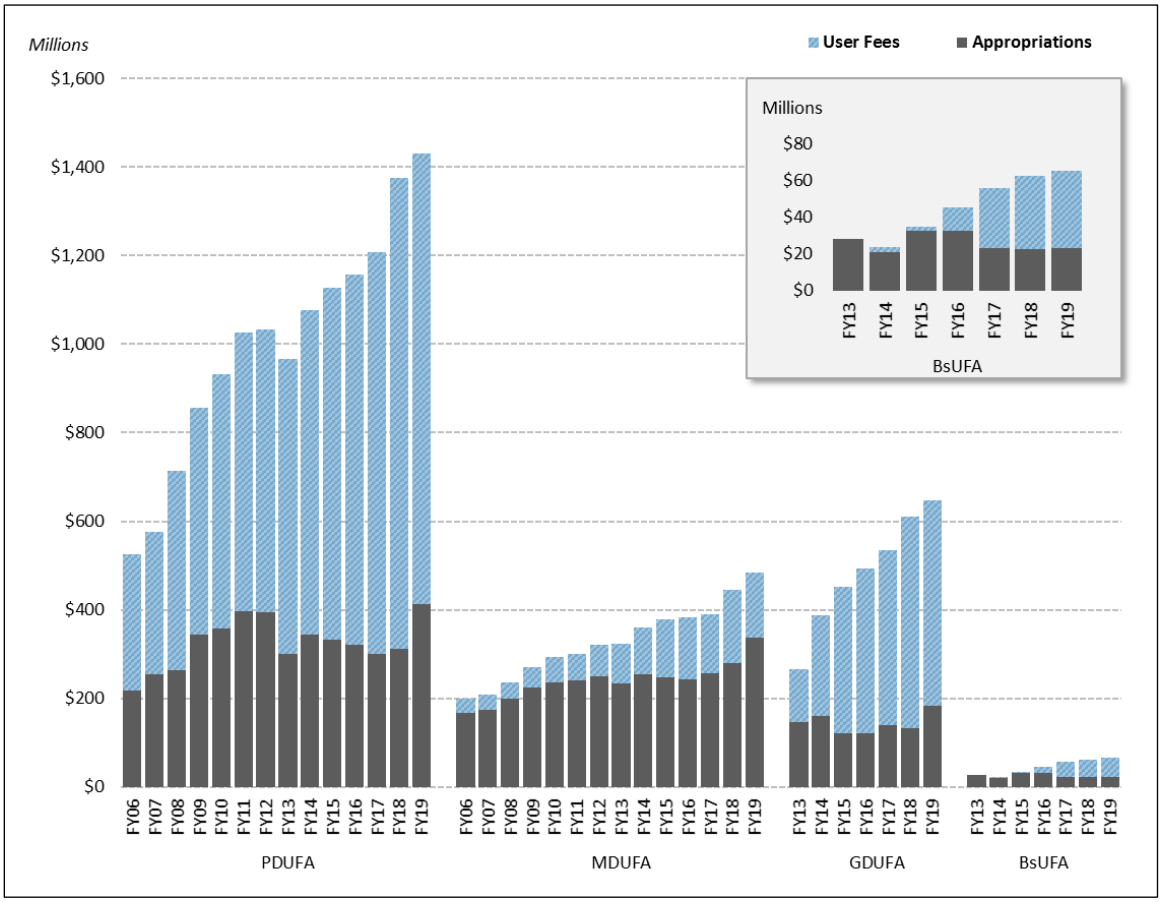
	PDUFA		MDUFA		GDUFA		BsUFA	
Original authorizing legislation	Prescription Drug User Fee Act of 1992 (P.L. 102-571)		Medical Device User Fee and Modernization Act of 2002 (P.L. 107-250)		Generic Drug User Fee Amendments of 2012 (Title III of FDASIA, P.L. 112-144)		Biosimilar User Fee Act of 2012 (Title IV of FDASIA, P.L. 112-144)	
Number of authorizations	6		4		2		2	
Sections in FFDCA	735, 736, 736B		737, 738, 738A		744A, 744B, 744C		744G, 744H, 744I	
Percent of program budget paid by user fees in FY2019	71%		30%		72%		64%	
Total FTEs in FY2019	4,495		1,692		2,015		184	
Fee schedule for FY2021	Application w/ clinical data	$2,875,842	PMA, PDP, PMR, BLA	$365,657	ANDA	$196,868	Initial BPD	$102,494
			BLA efficacy supplement	$365,657	DMF	$69,921	Annual BPD	$102,494
	Application w/o clinical data	$1,437,921	Panel-track supplement	$274,243	API domestic facility	$41,671	Reactivation	$204,988
			De Novo	$109,697	API foreign facility	$56,671	Application w/ clinical data	$1,746,745
			180-day supplement	$54,849	FDF domestic facility	$184,022		
	Program	$336,432	Real-time supplement	$25,596	FDF foreign facility	$199,022	Application fee w/o clinical data	$873,373
			510(k) submission	$12,432	CMO domestic	$61,341	Program	$304,162
			30-Day Notice	$5,851	CMO foreign	$76,341		
			Request for classification	$4,936	Program large	$1,542,993		
			Periodic report	$12,798	Program medium	$617,197		
			Establishment	$5,546	Program small	$154,299		

Source: FY2019 FDA User Fee Financial Reports; 85 *Federal Register* 46651, *Prescription Drug User Fee Rates for Fiscal Year 2021*, August 3, 2020; 85 *Federal Register* 46673, *Medical Device User Fee Rates for Fiscal Year 2021*, August 3, 2020; 85 *Federal Register* 46662, *Generic Drug User Fee Rates for Fiscal Year 2021*, August 3, 2020; 85 *Federal Register* 47220, *Biosimilar User Fee Rates for Fiscal Year 2021*, August 4, 2020.

Notes: ANDA, abbreviated new drug application; API, active pharmaceutical ingredient; BLA, biologics license application; BPD, biosimilar biological product development; CMO, Contract Manufacturing Organization; DMF, drug master file; FDASIA, FDA Safety and Innovation Act; FDF, final dosage form; FFDCA, Federal Food, Drug, and Cosmetic Act; FTE, full-time equivalent (employees); NDA, new drug application; PDP, product development protocol; PMA, premarket approval application; PMR, postmarket report; w/, with; w/o, without. The MDUFA fees listed are the standard fees, not the small business fees.

Appendix B. User Fees and Appropriations

Figure B-1. FDA Human Medical Product User Fee Programs: Total Costs, by Funding Source



Sources: Graphic created by CRS using data from FY2019 FDA User Fee Financial Reports at https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/default.htm; PDUFA Financial Report, Table 8, p. 17; MDUFA Financial Report, Table 8, p. 15; GDUFA Financial Report, Table 8, p. 16; BsUFA Financial Report, Table 8, p. 16.

Appendix C. Selected CRS Products Related to FDA Regulation of Human Medical Products

- CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*
- CRS In Focus IF11083, *Medical Product Regulation: Drugs, Biologics, and Devices*
- CRS Report R44576, *The Food and Drug Administration (FDA) Budget: Fact Sheet*
- CRS Report R44961, *FDA Reauthorization Act of 2017 (FDARA, P.L. 115-52)*
- CRS Report R44720, *The 21st Century Cures Act (Division A of P.L. 114-255)*
- CRS Report R44864, *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI*
- CRS Report R44517, *The FDA Medical Device User Fee Program: MDUFA IV Reauthorization*
- CRS Report R44703, *Generic Drugs and GDUFA Reauthorization: In Brief*
- CRS Report R44620, *Biologics and Biosimilars: Background and Key Issues*

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