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FDA Medical Product User Fee Reauthorization: In Brief

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Contents

Figures

Tables

Appendixes

Contacts

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 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.

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. User fees are authorized in legislation on a five-year cycle, with authority for their actual collection and expenditure provided each year through the annual appropriations process.[3]

FDA Premarket 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.

The four user fee programs discussed in this report are prescription drugs, medical devices, generic drugs, and biosimilars.[4] Congressional authorization for these four FDA user fee programs will expire at the end of FY2017 (September 30, 2017). The prescription drug user fee program was the first to be authorized; legislation first authorizing the four user fee programs is listed below:

- The Prescription Drug User Fee Act of 1992 (PDUFA, P.L. 102-571);[5]
- The Medical Device User Fee and Modernization Act of 2002 (MDUFMA, P.L. 107-250);[6]
- 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);[7]

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

[2] For more information about the regulation of prescription drugs and medical devices, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by (name redacted) and CRS Report R42130, *FDA Regulation of Medical Devices*, by (name redacted) .

[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*, by (name redacted) .

[4] The FDA also has user fee authorities for animal drugs, tobacco products, priority review, food reinspection, food recall, voluntary qualified food importer, and, most recently, 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.

[5] For more information, see CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): 2012 Reauthorization as PDUFA V*, by (name redacted)

[6] For more information, see CRS Report R44517, *The FDA Medical Device User Fee Program: MDUFA IV Reauthorization*, by (name redacted) .

[7] For more information, see CRS Report R44703, *Generic Drugs and GDUFA Reauthorization: In Brief*, by Judith A. (continued...)

- The Biosimilar User Fee Act of 2012 (BsUFA, Title IV of FDASIA, P.L. 112-144).[8]

A shared element of all four user fee programs is that the user fees are to supplement congressional appropriations, not replace them. The 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.[9] 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, Congress added preclinical drug development and certain postmarket activities to the allowable activities that may be paid for with user fee revenue. **Table A-1** in **Appendix A** outlines several elements of the four user fee programs, and **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.

In exchange for paying user fees, industry receives from FDA a commitment to meet performance goals, such as completing premarket review within a specified timeframe. At the beginning of 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. Current law requires the HHS secretary to submit each of the four user fee agreements to Congress by January 15, 2017, for this reauthorization cycle. In the past, Congress has accepted unchanged the terms and conditions as negotiated between FDA and the industry.

For the 2017 user fee program reauthorization cycle, draft performance goals have been agreed upon for all four user fee programs. These include in some cases a summary document, in addition to the performance goals document, containing statutory language (for MDUFA) and the fee structure (for GDUFA). Links to all four performance goal documents, and the two summary documents, are provided in the text box below.

User Fee Draft Performance Goals for Cycles to Begin October 1, 2017

PDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf

GDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf; http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525236.pdf

MDUFA: http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526395.pdf; http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526532.pdf

BsUFA: http://www.fda.gov/ForIndustry/UserFees/BiosimilarUserFeeActBsUFA/default.htm

Due to the importance of user fees to FDA's budget, reauthorization of the user fee programs is considered "must pass" legislation. Congress generally uses the reauthorization bill to address

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Johnson.

[8] For more information, see CRS Report R44620, *Biologics and Biosimilars: Background and Key Issues*, by (name redacted) .

[9] FFDCA 736(f) and (g); FFDCA 738(h) and (i); FFDCA 744B(h) and (i); FFDCA 744H(e). 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.

related FDA regulatory concerns; it therefore serves as an important driver for the ongoing modification of overall agency regulatory policy. However, recent passage of the 21st Century Cures Act (Division A, P.L. 114-255) included sections that modified drug and device regulation, perhaps reducing the number of such provisions to be added to the user fee reauthorization bill.[10]

The last user fee reauthorization occurred in July 2012, with the passage of FDASIA.[11] The law consists of 11 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. FDASIA Titles V through IX addressed a range of other policy issues including pediatric drug research, medical device regulation, pharmaceutical supply chain security, antibiotic development incentives, expedited drug approval, drug shortages, and a set of miscellaneous provisions.

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.[12] 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. FDA's *total program level* increased from $3.832 billion in FY2012 to $4.745 billion in FY2016. Although congressionally appropriated funding increased by 9% over that time period, user fee revenue increased more than 50%. All user fees accounted for 43% of FDA's enacted FY2016 *total program level*.[13]

FDA's Human Drugs Program is responsible for ensuring the safety and effectiveness of new and generic prescription drugs, over-the-counter (OTC) drug products, and therapeutic biologics; monitoring marketed drug products to ensure patient safety; and monitoring drug quality.[14] In FY2016, all user fees accounted for 64.7% of the Human Drugs Program enacted total program level, including revenue from PDUFA, GDUFA, and BsUFA user fees.[15] The following paragraphs look at 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 FY2006, prescription drug user fees provided 58% of the PDUFA program total costs (appropriations provided 42%); in FY2015, user fees covered 71% of PDUFA program total costs (appropriations covered 29%).[16] While most of PDUFA revenue supports activities managed by CDER, PDUFA

[10] For more information about the 21st Century Cures Act, see CRS Report R44720, *The 21st Century Cures Act (Division A of P.L. 114-255)*, coordinated by (name redacted) .

[11] For more information about FDASIA, see CRS Report R42680, *The Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144)*, coordinated by (name redacted)

[12] 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*, by (name redacted) and (name redacted)

[13] The FY2016 user fee amounts reflect what the congressional committees have authorized FDA to collect and spend that fiscal year. However, there is generally variation between the enacted amount and the amount that is spent from user fees. The amounts in the "Actual" column in the FDA *Justification of Estimates for Appropriations Committees* (CJ) reflect the amount spent from PDUFA fees, corresponding to the columns labeled "Obligations" and "Amount spent from ... fees" in the FDA user fee financial reports.

[14] FDA, Human Drugs, Narrative by Activity, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM488553.pdf.

[15] 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*, by (name redacted) and (name redacted)

[16] FDA, *FY2015 PDUFA Financial Report*, Table 8: PDUFA Program—Historical Trend of Total Costs by Funding (continued...)

revenue also contributes to other FDA organizational components that support the PDUFA program, including CBER, the Office of Regulatory Affairs (ORA), and FDA headquarters.[17]

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 FY2006, medical device user fees accounted for 16% of the MDUFA program total costs, compared with 35% in FY2015.[18] 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.[19]

GDUFA is currently completing its first authorization cycle; FY2013 was the first year for which user fee amounts were available. In FY2013, user fees accounted for 45% of the GDUFA program total costs compared with 73% in FY2015.[20] 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.[21]

Like GDUFA, BsUFA is currently in its first authorization cycle; FY2013 was the first year for which user fee amounts were available. In FY2013, user fees accounted for 0% of the BsUFA program total costs compared with 7% in FY2015.[22] Like the other three user fee programs, 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.[23]

Medical Product User Fee Programs

PDUFA

Prior to marketing, a manufacturer must submit a new drug application (NDA) to FDA, demonstrating the drug's safety and effectiveness. FDA scientific and regulatory personnel review the NDA and prepare written assessments in several categories—medical, chemistry, statistical,

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Source as of September 30 of each Fiscal Year, p. 13, at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/PDUFA/UCM499021.pdf.

[17] Ibid., Table 7: PDUFA Program—Historical Trend of Total Costs by Organization as of September 30 of Each Fiscal Year, p. 12.

[18] FDA, *FY2015 MDUFA Financial Report*, Table 7: MDUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of each Fiscal Year, p. 12, at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/MDUFMA/UCM500460.pdf.

[19] Ibid., Table 6: MDUFA Program—Historical Trend of Total Costs by Organization as of September 30 of Each Fiscal Year, p. 11.

[20] FDA, *FY2015 GDUFA Financial Report*, Table 7: GDUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of Each Fiscal Year, p. 10, at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/GDUFA/UCM498940.pdf.

[21] Ibid., Table 6: GDUFA Program—Historical Trend of Total Costs by Organization as of September 30 of Each Fiscal Year, p. 10.

[22] FDA, *FY2015 BsUFA Financial Report*, Table 6: BsUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of Each Fiscal Year, p. 10, at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/UCM494948.pdf.

[23] Ibid., Table 5: BsUFA Program—Historical Trend of Total Costs by Organization as of September 30 of Each Fiscal Year, p. 9.

pharmacology, clinical pharmacology and biopharmaceutics, risk assessment and risk mitigation, proprietary name, patient labeling—and then decide whether or not to approve the drug.[24]

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."[25] That five-year authority, which covered both NDAs and biologics license applications (BLAs),[26] has been renewed on four subsequent occasions, by PDUFA II (1997), PDUFA III (2002), PDUFA IV (2007), and PDUFA V (2012). The most recent reauthorization was Title I of FDASIA, which extended the user fee program through September 30, 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. With each reauthorization, 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).
- PDUFA II expanded the range of activities for which FDA could use prescription drug user fee revenue to include those related to the clinical trial phases of a new drug's development.
- PDUFA III extended the range of activities for which FDA could use prescription drug user fee revenue to include both a drug's preclinical development period and three years into the postapproval and marketing period.
- PDUFA IV removed the three-year limitation on postapproval activities, and again expanded the list of postmarket safety activities that the fees could support (e.g., developing and using adverse-event data-collection systems, implementing and enforcing new FFDCA requirements relating to postapproval studies, clinical trials, labeling changes, and risk evaluation and mitigation strategies).
- PDUFA V maintained the PDUFA IV scope of activities that PDUFA fees could support.

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. The law specifies certain exemptions and waivers (orphan drugs, small businesses) and requires that three types of fees each contribute one-third of the total fee revenue each year:

- *Application fee*: A drug's sponsor (usually the manufacturer) must pay a fee for FDA review each time it submits an NDA for a new drug, a supplemental application for a major change to an already approved NDA,[27] or a BLA.
- *Establishment fee*: Each manufacturer must pay an annual fee for each of its manufacturing establishments.

[24] 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.

[25] P.L. 102-571.

[26] A biologics license application (BLA) refers to an application submitted to FDA for the licensure of certain biological products under Section 351 of the Public Health Service Act (PHS Act).

[27] A supplemental application means a request to FDA to approve a change (e.g., a new indication/use) to an approved NDA.

- *Product fee*: Manufacturers must pay an annual fee for each product that fits within PDUFA's definition.

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 with micro-chip technology and laser surgical devices."[28] Medical devices also include in vitro diagnostic products, reagents, test kits, and certain electronic radiation-emitting products with medical applications, such as diagnostic ultrasound products, x-ray machines, and medical lasers. 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.

The FFDCA requires premarket review for moderate- and high-risk devices. There are two main paths manufacturers can use to bring a device to market. One path consists of conducting clinical studies and submitting a premarket approval (PMA) application that includes evidence providing reasonable assurance that the device is safe and effective. A successful PMA process results in device *approval*. In FY2015, 98% of PMAs accepted for filing were approved by FDA.[29]

The other path involves submitting a 510(k) notification demonstrating that the device is substantially equivalent to a device already on the market (a predicate device) that does not require a PMA. The 510(k) process is unique to medical devices and, if successful, results in FDA *clearance*. The 510(k) process is less costly and time-consuming than the PMA path. Substantial equivalence is determined by comparing the performance characteristics of a new device with those of a predicate device. Demonstrating substantial equivalence does not usually require submitting clinical data demonstrating safety and effectiveness. According to FDA data, 85% of 510(k)s accepted for review in FY2015 were determined to be substantially equivalent.[30]

Congress first gave FDA the authority to collect user fees from the medical device industry in 2002. That authority has been renewed twice by MDUFA II (2007) and MDUFA III (2012). Low-risk medical devices (class I) and a small number of moderate-risk (class II) medical devices are exempt from premarket review and payment of the associated fee. Of the unique devices that are listed by manufacturers with FDA in FY2016, about 63% were exempt from premarket review, 35% entered the market via the 510(k) process and 1% via the PMA process. FDA typically evaluates about 4,000 510(k) notifications and 40 original PMA applications each year.[31]

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

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

[29] 1st Quarter FY2016 Package, MDUFA III (FY2013-2017) Performance, February 18, 2015, p. 22, at http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM487953.pdf.

[30] 1st Quarter FY2016 Package, MDUFA III (FY2013-2017) Performance, February 18, 2015, p. 199, at http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM487953.pdf.

[31] U.S. Congress, Senate Special Committee on Aging, A Delicate Balance: FDA and the Reform of the Medical Device Approval Process, Testimony of William Maisel, Deputy Center Director for Science, FDA/CDRH, 112th Cong., 1st sess., April 13, 2011. For more current data, see 1st Quarter FY2016 Package, MDUFA III (FY2013-2017) Performance, February 18, 2015, PMA data on pp. 23-32, 510(k) data on pp. 201-210, at http://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM487953.pdf.

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 high-risk (class III) devices for which periodic reporting is required. MDUFA II also added two additional types of application fees[32] 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. Other than the establishment fee, the amount of each type of user fee is 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 III changed the 510(k) fee from 1.84% of the PMA fee to 2% of the PMA fee and the PMA fee amount from $248,000 in FY2013 to $268,443 in FY2017 (prior to inflation adjustment). MDUFA III adjusted the total revenue amounts by a specified inflation adjustment, similar to the adjustment made under PDUFA, and the base fee amount is adjusted as needed on a uniform proportional basis to generate the inflation-adjusted total revenue amount. After the base fee amounts are adjusted for inflation, the establishment fee amount is further adjusted as necessary so that the total fee collections for the fiscal year generates the total adjusted revenue amount.

- *Application fees:* The sponsor of a PMA, a 510(k) submission, or a supplement (panel-track, 180-day, real-time) must pay a fee for each submission.
- *Establishment fees*: Sponsors whose establishment meets the MDUFA III definition must pay an annual registration fee.
- *Periodic reporting fee*: Sponsors of certain class III devices must pay an annual fee.

GDUFA

Since the Hatch-Waxman amendments to the FFDCA in 1984,[33] FDA has approved generic drugs, allowing safe and effective alternatives to brand-name prescription drugs. Because the brand-name sponsor has already submitted evidence to FDA supporting a drug's safety and effectiveness based on clinical trial data, the sponsor of a generic drug may ask FDA to rely on those data. Rather that submit data from animal studies, clinical studies, and bioavailability, the generic sponsor must show that the generic product is bioequivalent to the brand-name product. FDA still requires the generic sponsor to submit to reviews of chemistry, manufacturing, controls, labeling, and testing. 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.

A 2016 report sponsored by the Generic Pharmaceutical Association (GPhA) states that generic drugs have saved the U.S. health system $1.46 trillion from 2006 to 2015.[34] "Generics are 89% of

[32] The two applications are (1) the 30-Day Notice, used by a manufacturer to request modifications in manufacturing procedures, and (2) the 513(g) application, used by a manufacturer to request information on device classification.

[33] 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. In the ANDA, the generic company establishes that its drug product is chemically the same as the already approved drug and thereby relies on the FDA's previous finding of safety and effectiveness for the approved drug.

[34] The Generic Pharmaceutical Association, *2016 Generic Drug Savings & Access in the United States Report*, at http://www.gphaonline.org/media/generic-drug-savings-2016/index.html.This, the eight annual report, was compiled by Quintiles IMS Institute for GPhA.

prescriptions dispensed but only 27% of total drug costs. Put another way, brand drugs are only 11% of prescriptions but are responsible for 73% of drug spending."[35] However, with an increase in the number of abbreviated new drug applications (ANDAs) submitted to FDA for review, and an increase in the number of foreign facilities making generic drugs, the agency lacked the resources to keep pace, resulting in a backlog of submitted ANDAs.

Prior to the passage of GDUFA, 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. GDUFA authorized FDA to collect fees from generic drug companies to supplement the cost of certain human generic drug activities, including review of ANDAs and drug master files (DMFs);[36] approval, deficiency, and complete response letters; facility inspections; monitoring or research; postmarket safety activities; and regulatory science.

In exchange, FDA committed to meeting certain performance goals.[37] Under GDUFA, the agency also committed 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.

The first five-year authorization of GDUFA 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. The law established a one-time backlog fee for ANDAs pending as of October 1, 2012, and three types of user fees to contribute to the total fee revenue each year:

- *Drug Master File fee*: The sponsor of a Type II active pharmaceutical ingredient (API)[38] DMF in a generic drug submission must pay an annual fee for each DMF.
- *Application fee*: The sponsor of an ANDA or a prior approval supplement (PAS) to an approved ANDA must pay a fee for each submission.
- *Facility fee*: Generic drug manufacturers must pay an annual fee for each manufacturing establishment.

BsUFA

A biologic drug is made from living organisms. Compared with conventional chemical drugs, biologic drugs are relatively large and complex molecules. A biosimilar is a therapeutic drug that is similar but not structurally identical to the brand-name biologic drug made by a pharmaceutical or biotechnology company. Biologics and biosimilars frequently require special handling and processing to avoid contamination (by microbes or other unwanted substances) and are usually administered to patients via injection or infused directly into the bloodstream. For these reasons, biologics often are referred to as specialty drugs.

[35] Ibid.

[36] 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.

[37] Generic Drug User Fee Act Program Performance Goals and Procedures, "GDUFA Commitment Letter."

[38] 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.

The cost of specialty drugs, including biologics, can be very high. The introduction of biosimilars in 2006 in Europe has reduced prices for biologics overall, in some cases by 33% compared with the original price of the brand-name product.[39] Marketing biosimilars in the United States became possible in March 2010 when Congress established a new regulatory authority for FDA by creating an abbreviated licensure pathway for biological products demonstrated to be "highly similar" (biosimilar) to, or "interchangeable" with, an FDA-licensed biological product. This new authority, the Biologics Price Competition and Innovation Act (BPCIA) of 2009, was enacted as Title VII of the Affordable Care Act (ACA, P.L. 111-148). Authority to collect user fees was provided by the Biosimilar User Fee Act of 2012 (BsUFA, Title IV of FDASIA, P.L. 112-144).

The biosimilars user fee program allows FDA to collect six types of fees from industry. Fee amounts are based on inflation-adjusted PDUFA fee amounts for each fiscal year. Because no marketed biosimilar products existed when the BsUFA program started, it included fees for products in the development phase to generate fee revenue for the new program and to enable companies to meet with FDA in the early development of biosimilar products. A company may choose to discontinue participation in the biosimilar product development program but must pay a reactivation fee to resume further product development with FDA. BsUFA fees are as follows:

- *Initial product development fee:* The sponsor of a biosimilar must pay a fee for development meetings with FDA or when submitting a clinical protocol.
- *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—or a supplemental application for a change to an approved application—minus the cumulative amount paid for: the initial development fee, the annual product development fee, and any reactivation fee.
- *Establishment fee*: Each applicant named in a biosimilar application must pay an annual fee for each establishment that manufactures the biosimilar in final dosage form.
- *Product fee*: The sponsor of a biosimilar biological product application must pay an annual fee for each such 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.

[39] IMS Health, *The Impact of Biosimilar Competition*, June 2016, p. 4, at http://ec.europa.eu/growth/tools-databases/newsroom/cf/itemdetail.cfm?item_id=8854.

Appendix A. FDA Human Medical Product User Fee Programs

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

Prescription Drugs, Medical Devices, Biosimilars, and Generic Drugs

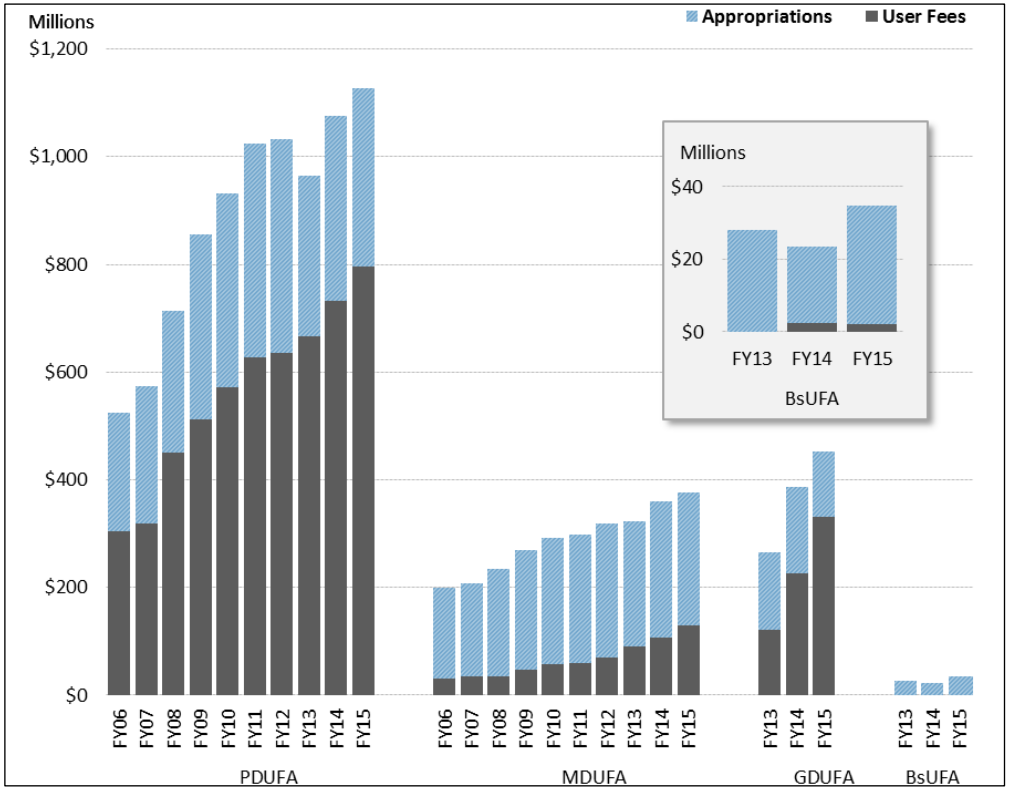
	PDUFA		MDUFA		BsUFA		GDUFA	
Original authorizing legislation	Prescription Drug User Fee Act of 1992 (P.L. 102-571)		Medical Device User Fee and Modernization Act of 2002 (P.L. 107-250)		Biosimilar User Fee Act of 2012 (Title IV of FDASIA, P.L. 112-144)		Generic Drug User Fee Amendments of 2012 (Title III of FDASIA, P.L. 112-144)	
Number of reauthorizations	5		3		None		None	
Percent of program budget paid by user fees in FY2015	71%		35%		7%		73%	
Total FTEs in FY2015	4,138		1,592		153		1,397	
Fee schedule for FY2017	Application w/ clinical data	$2,038,100	PMA, PDP, PMR, BLA	$234,495	Initial development	$203,810	ANDA	$70,480
			BLA efficacy supplement	$234,495	Annual development	$203,810	PAS	$35,240
	Application w/o clinical data	$1,019,050	Panel-track supplement	$175,871	Reactivation	$407,620	DMF	$51,140
			180-day supplement	$35,174	Application w/ clinical data	$2,038,100	API domestic facility	$44,234
	Supplement w/ clinical data	$1,019,050	Real-time supplement	$16,415	Application fee w/o clinical data	$1,019,050	API foreign facility	$59,234
			510(k) submission	$4,690	Supplement w/ clinical data	$1,019,050	FDF domestic facility	$258,646
	Establishment	$512,200	30-Day Notice	$3,752	Establishment	$512,200	FDF foreign facility	$273,646
			Classification fee	$3,166	Product	$97,750		
	Product	$97,750	Periodic annual report	$8,207				
			Establishment annual fee	$3,382				

Source: FY2015 FDA User Fee Financial Reports at http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/default.htm; 81 FR 49674, *PDUFA Rates for FY2017*, July 28, 2016; 81 FR 49987, *MDUFA Rates for FY2017*, July 29, 2016; 81 FR 49681, *BsUFA Rates for FY2017*, July 28, 2016; 81 FR 49225, *GDUFA Rates for FY2017*, July 27, 2016.

Notes: ANDA, abbreviated new drug application; API, active pharmaceutical ingredient; BLA, biologics license application; DMF, drug master file; FDASIA, FDA Safety and Innovation Act; FDF, final dosage form; FTE, full-time equivalent (employees); NDA, new drug application; PAS, prior approval supplement; PDP, product development protocol; PMA, premarket approval application; PMR, postmarket report; w/, with; w/o, without.

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 the following FDA reports: FDA, FY2015 PDUFA Financial Report, Table 8: PDUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of each Fiscal Year, p. 13; FDA, FY2015 MDUFA Financial Report, Table 7: MDUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of each Fiscal Year, p. 12; FDA, FY2015 GDUFA Financial Report, Table 7: GDUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of Each Fiscal Year, p. 10; FDA, FY2015 BsUFA Financial Report, Table 6: BsUFA Program—Historical Trend of Total Costs by Funding Source as of September 30 of Each Fiscal Year, p. 10.

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