



Prescription Drug User Fee Act (PDUFA): 2012 Reauthorization as PDUFA V

Susan Thaul
Specialist in Drug Safety and Effectiveness

February 22, 2013

Congressional Research Service

7-5700

www.crs.gov

R42366

Summary

Title I of the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144) reauthorized the Prescription Drug User Fee Act (PDUFA) through September 30, 2017. Known as PDUFA V, this was the program's fourth five-year reauthorization. The Prescription Drug User Fee Act (PDUFA), in 1992, gave the Food and Drug Administration (FDA) the authority to collect fees from the pharmaceutical industry and to use the revenue to support "the process for the review of human drug applications."

PDUFA fees provided 52% of the Human Drugs Program funding for FY2012, accounting for more than 2,000 full-time equivalent employees. Therefore, as each reauthorization deadline approaches, FDA, industry groups, and most Members of Congress see PDUFA as must-pass legislation. Congress originally intended PDUFA to diminish the backlog of new drug applications at FDA and shorten the time from submission to decision. The general view is that PDUFA has succeeded. FDA has added review staff and reduced its review times. At each reauthorization, however, discussion returns to certain issues in the context of PDUFA that also reflect broader FDA concerns. The issues—and results—differ. PDUFA II expanded the user fee program's scope to include activities related to the investigational phases of a new drug's development, and to increase FDA communications with industry and consumer groups. PDUFA III again expanded the scope of activities that user fees could support to include both preclinical development and a three-year postapproval period. PDUFA IV concentrated on new measures concerning postmarket drug safety.

The PDUFA V statutory language does not differ much from PDUFA IV. The accompanying FDA-industry agreement on performance and goals and procedures for FY2013 through FY2017 includes revised communication procedures and timing goals during the application review process and addresses expanded FDA efforts in regulatory science, drug development, drug safety, and information technology.

In addition to PDUFA reauthorization, FDASIA included 10 other titles that reauthorized medical device user fees, established generic drug and biosimilar biological product user fees, and addressed pediatric drug research, medical device regulation, pharmaceutical supply chain security, antibiotic development incentives, expedited drug approval, drug shortages, and a set of miscellaneous provisions.

Contents

Introduction.....	1
Origin of Prescription Drug User Fees	2
Current Law	2
PDUFA Impact on FDA Review Time and Budget	6
Review Time.....	6
Budget	7
PDUFA V Package.....	9
Statutory Language.....	9
Industry-FDA Performance Goals and Procedures for PDUFA V: The Agreement	10
PDUFA Reauthorization as Driver of FDA Legislation	11

Figures

Figure 1. Drug Research and Development Path and PDUFA Coverage	4
Figure 2. Median Approval Times, New Molecular Entities (NMEs) and New Biologic Entities (NBEs), by Fiscal Year of Receipt.....	7
Figure 3. FDA Human Drugs Program Budget, by Funding Source, for FY1990 through FY2012	8

Tables

Table 1. FDA Human Drugs Program, Fees as a Percentage of Total Program Level for Selected Fiscal Years	8
Table A-1. Provisions in Sections 735 and 736 of the Federal Food, Drug, and Cosmetic Act Relating to Prescription Drug User Fees: Definitions and Authority to Assess and Use Drug Fees	12
Table A-2. Provisions in Section 736B of the Federal Food, Drug, and Cosmetic Act Relating to Prescription Drug User Fees: Reauthorization; Reporting Requirements.....	15
Table B-1. Performance Goals and Procedures in Agreement Between FDA and Industry Representatives for FY2013 through FY2017 Under PDUFA V	16
Table B-2. FDA Commitments to Produce Guidance Documents and Hold Public Meetings and Workshops, FY2013-FY2017	21

Appendixes

Appendix A. Provisions in FFDCA Sections 735, 736, and 736B	12
Appendix B. PDUFA V Agreement: Performance Goals and Procedures.....	16

Contacts

Author Contact Information..... 21

Introduction

The Prescription Drug User Fee Act (PDUFA I), in 1992, gave the Food and Drug Administration (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.”¹ That authority, which expired in 1997, has been renewed on four subsequent occasions, by PDUFA II (1997), PDUFA III (2002), PDUFA IV (2007), and PDUFA V (2012). This most recent reauthorization was Title I of the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144); it extends the user fee program through September 30, 2017.

For FY2012, 35% of FDA’s total budget came from user fees;² however, prescription drug fee revenue provided 51% of FDA’s Human Drugs Program budget.³ PDUFA revenue also contributed to the Biologics Program,⁴ and agency-wide headquarters and rent budgets.

Congress first passed PDUFA to supplement the FDA budget outside of the appropriations process. The added funds would allow the agency to increase its staff so it could finish new drug application reviews sooner, allowing both earlier patient access to new drugs and earlier industry earnings on those drugs. PDUFA I amended the Federal Food, Drug, and Cosmetic Act (FFDCA) to establish the authority and the process for collecting and using industry fees;⁵ it also required FDA and industry representatives to agree on the performance goals and procedures that the PDUFA revenue would support.

For the 2012 reauthorization, FDA posted a draft agreement on its website on September 1, 2011, noting that it was subject to review by the Department of Health and Human Services (HHS) and the Office of Management and Budget (OMB). On January 13, 2012, the HHS Secretary submitted both draft legislative language and the agreed-upon performance goals document (the Agreement) to Congress.⁶ The House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions, which have jurisdiction over the PDUFA

¹ P.L. 102-571. After Congress first reauthorized PDUFA in 1997, the initial law became known as PDUFA I.

² In addition to PDUFA’s prescription drug user fees, Congress has authorized user fees for medical devices, animal drugs, animal generic drugs, tobacco products, mammography, color and export certification, and, most recently, several foods-related programs. See Department of Health and Human Services (HHS), *Fiscal Year 2013 Food and Drug Administration: Justification of Estimates for Appropriations Committees*, “FY2013 CJ All Purpose Table—User Fees,” <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM298349.pdf>.

³ Of the \$702 million in PDUFA fees for FY2012, 71% went to the Human Drugs Program (funding 2,031 full-time equivalent employees (FTEs)), 15% to the Biologics Program (360 FTEs), and 14% to headquarters (195 FTEs) and rent (Department of Health and Human Services, *Fiscal Year 2013 Food and Drug Administration: Justification of Estimates for Appropriations Committees*, page 94 [PDF page 101], <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM291555.pdf>).

⁴ Biologics are medical preparations made from living organisms. Examples of such products include traditional biologics (such as vaccines, blood, blood products, antitoxins, and allergenics) and human therapeutic agents produced by the biotechnology industry (such as insulin, interferon, growth hormone, and epoetin).

⁵ The Prescription Drug User Fee Act (PDUFA), in 1992, added Sections 735 and 736 to the Federal Food, Drug, and Cosmetic Act (FFDCA) [21 U.S.C. 379g and 379h]. In 2007, PDUFA IV added FFDCA Sections 736A and 736B [21 U.S.C. 379h-1 and 379h-2].

⁶ FDA, “FDA completes work on three drug user fee programs,” FDA News Release, January 13, 2012, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm287723.htm>; “FDA V Statutory Language,” <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM287747.pdf>; and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2012 through 2017,” <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>.

reauthorization, held hearings and marked up legislation to extend the prescription drug user fee authority. The PDUFA reauthorization became Title I of the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144), whose other 10 titles covered reauthorization of medical device user fees, new authorities for generic drug and biosimilar biological product user fees, and other topics such as pediatric drug research, medical device regulation, pharmaceutical supply chain security, antibiotic development incentives, expedited drug approval, drug shortages, and a set of miscellaneous provisions.⁷

This report describes (1) the origin of prescription drug user fees; (2) current law; (3) the impact of PDUFA on FDA application review time and the agency's Human Drugs Program budget; and (4) the PDUFA V package (legislative language and the performance goals Agreement).

Origin of Prescription Drug User Fees

In the late 1980s, the median time for FDA to approve a new drug application (NDA) was 29 months. Industry, consumer groups, and FDA agreed that the time from submission of a drug or biologics application to FDA's decision was unacceptably long. Patient advocates argued that a drug in review—and therefore not available for sale—could be the difference between life and death. Manufacturers argued that prolonged review times affected their ability to recoup the costs of research and development. During PDUFA I consideration, FDA estimated that each one-month delay in a review's completion cost a manufacturer an average of \$10 million.⁸

FDA argued that it needed more scientists to review the drug applications that were coming in and the ones already backlogged in its files and that it had insufficient appropriations to hire additional scientists to conduct reviews. For decades FDA had asked Congress for permission to implement user fees; the pharmaceutical industry generally opposed them, believing the funds might go into the Treasury to reduce federal debt rather than help fund drug review.⁹

The 1992 law became possible when the then FDA commissioner David Kessler worked out an arrangement that met two industry demands: performance goals, which would set target completion times for various review processes; and the promise that these fees would supplement—rather than replace—funding that Congress appropriated to FDA. Those steps helped persuade industry groups the fees would reduce review times—and paved the way for Congress to authorize a revenue source that FDA had sought for over 20 years.

Current Law

PDUFA I—and the subsequent PDUFA II, PDUFA III, PDUFA IV, and PDUFA V—authorized the collection of prescription drug user fees and the use of that revenue for specified activities.

⁷ For a description of provisions in the Food and Drug Administration Safety and Innovation Act, see CRS Report R42680, *The Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144)*, coordinated by Susan Thaul.

⁸ Philip J. Hilts, "Plan to Speed Approval of Drugs: Makers Would Pay Fees to U.S.," *New York Times*, August 11, 1992, page A1.

⁹ Philip J. Hilts, *Protecting America's Health: The FDA, Business, and One Hundred Years of Regulation*, New York: Alfred A. Knopf, 2003, page 278.

This section of the report presents a brief overview of current law; **Table A-1** in **Appendix A** provides additional detail, also noting significant additions or modifications across PDUFA reauthorizations.

PDUFA and Its Reauthorizations

PDUFA (PDUFA I)
Prescription Drug User Fee Act
P.L. 102-571, October 29, 1992

PDUFA II
Title I of the Food and Drug Administration Modernization Act (FDAMA)
P.L. 105-115, November 21, 1997

PDUFA III
Title V of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002
P.L. 107-188, June 12, 2002

PDUFA IV
Title I of the FDA Amendments Act of 2007 (FDAAA)
P.L. 110-85, September 27, 2007

PDUFA V
Title I of the FDA Safety and Innovation Act (FDASIA)
P.L. 112-144, July 9, 2012

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 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 the FDA review each time it submits a new drug application or supplemental application, or a biologics license application.¹⁰
- *Establishment fee:* Each manufacturer must pay an annual fee for each of its manufacturing establishments.¹¹
- *Product fee:* Each manufacturer must pay an annual fee for each product that fits within PDUFA's definition.¹²

The latter two were designed to provide a more stable and predictable revenue source because the number of applications may vary from year to year. The law specifies, for all three fees, certain exemptions and waivers, such as for orphan drugs and small businesses.

A key element of PDUFA, carried throughout all reauthorizations, is that the user fees are to supplement congressional appropriations, not replace them. The law includes three limiting conditions, known as "triggers," to enforce that goal. FDA may collect and use fees only if the direct appropriations for the activities involved in the review of human drug applications and for

¹⁰ Examples of the application fee involving clinical data (in unadjusted dollars) for selected years, as announced in the Federal Register each year and based on the statutory limit (<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm152775.htm>) are: FY1993: \$100,000; FY1997: \$256,846; FY2002: \$313,320; FY2007: \$896,200; FY2012: \$1,841,500; and FY2013: \$1,958,800.

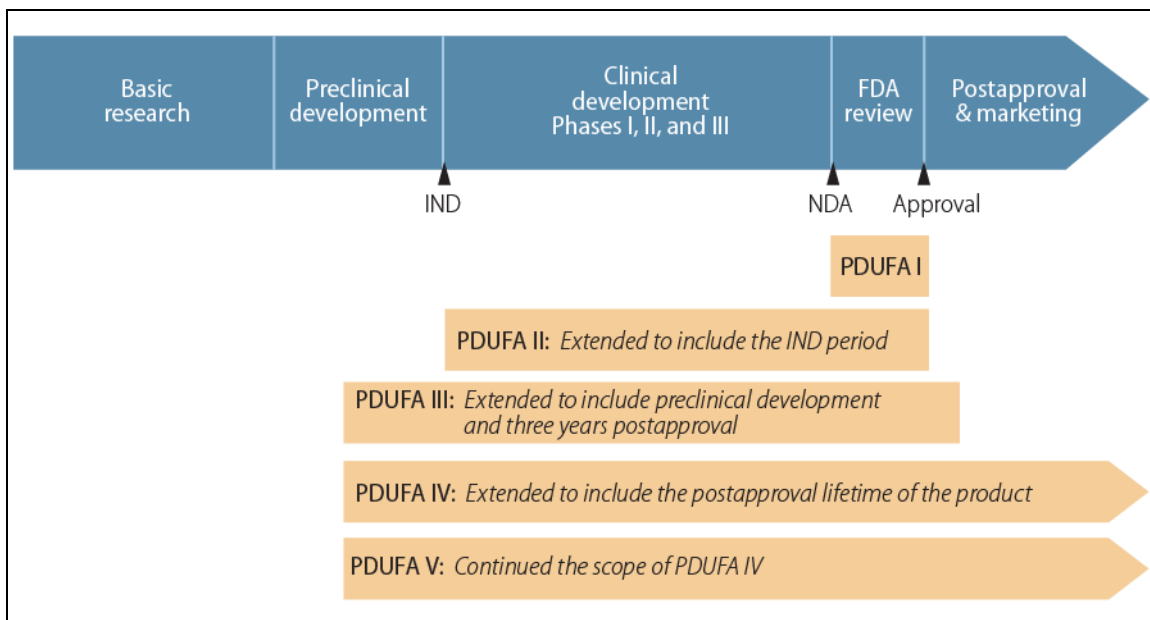
¹¹ The PDUFA establishment fee for FY2013 is \$526,000.

¹² The PDUFA product fee for FY2013 is \$98,380.

FDA activities overall remain at a level at least equal (adjusted for inflation) to the pre-PDUFA budget.¹³

PDUFA I authorized FDA to use the fee revenue to fund the “process for the review of human drug applications.” It defined what that process encompassed.¹⁴ With each reauthorization, Congress has amended that definition to expand the scope of activities covered by PDUFA. The upper portion of **Figure 1** depicts the research and development path of a new drug, from basic research, through preclinical development and testing on animals, clinical development in trials on human subjects as an investigational new drug (IND), FDA review of the new drug application (NDA), and, finally, the postapproval period in which the drug is marketed.¹⁵ The figure’s lower portion illustrates the segments of this path during which FDA may use PDUFA revenue to support its activities.

Figure 1. Drug Research and Development Path and PDUFA Coverage



Source: Prepared by CRS.

Notes: FDA=Food and Drug Administration. PDUFA=Prescription Drug User Fee Act. IND=Investigational new drug application. NDA=New drug application.

- PDUFA I allowed fee revenue to fund “activities necessary for the review of human drug applications and supplements.” In addition to the actual review of applications, it covered activities such as letters from FDA to applicants outlining deficiencies in their applications; facility inspections as part of pending approval applications; and monitoring of research necessary for the review of applications.

¹³ See the FDA’s *FY 2010 PDUFA Financial Report* for a detailed description of these conditions and related calculations, <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/PDUFA/ucm262845.htm>.

¹⁴ FDCA Section 735 [21 U.S.C. 379g].

¹⁵ For a description of the FDA drug approval process, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by Susan Thaul.

- All those activities fit within the time window from when a manufacturer submits a new drug application (NDA) until FDA makes its decision on that application.
- 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 (from the IND to submission of an NDA).
 - 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. It allowed FDA to use PDUFA revenue for the collection, development, and review of postmarket safety information for up to three years postapproval (for drugs approved after October 1, 2002). That change allowed the agency to double the number of staff monitoring side effects of drugs already on the market. It also allowed FDA to use fees to develop databases documenting drug use.
 - PDUFA IV removed the three-year limitation on postapproval activities, and again expanded the list of postmarket safety activities that the fees could support. New items on the list included developing and using adverse-event data-collection systems, including information technology systems; developing and using improved analytical tools to assess potential safety problems, including access to external databases; implementing and enforcing new FFDCA requirements relating to postapproval studies, clinical trials, labeling changes, and risk evaluation and mitigation strategies; and managing adverse event reports.
 - PDUFA V maintained the PDUFA IV scope of activities that PDUFA fees could support.¹⁶

PDUFA I connected prescription drug user fees to *performance goals and targets*. FDA negotiated those goals and targets with the pharmaceutical industry and presented them to Congress in the form of a letter from the HHS Secretary, to which the legislation referred without putting the letter's language in the FFDCA. PDUFA II and III continued that procedure, again referring to the letter ("PDUFA Reauthorization Performance Goals and Procedures"). PDUFA IV, in 2007, however, codified, as FFDCA Sec. 736B, the requirements for a goals letter, consultation and public communication, and other processes.¹⁷ A summary of this added FFDCA

¹⁶ FFDCA Section 735 defines the term "process for the review of human drug applications" as activities necessary for the review of human drug applications and supplements; the issuance of action letters; inspection of prescription drug establishments and other facilities; activities necessary for the review of applications for licensure of biological product establishments and for the release of lots of biologics; and monitoring of research conducted in connection with the review of human drug applications.

The term "costs of resources allocated for the process for the review of human drug applications" is defined as expenses and costs for FDA officers, employees, contractors, and advisory committees; information management; computer resources; facilities, furniture, equipment, materials and supplies; and collecting user fees and accounting for resources.

PDUFA IV added several items to the list of postmarket safety activities for which the fees could be used. These include adverse event data collection systems and improved analytical tools, increased requirements for adverse event reporting both to the Secretary and to the public, and enforcement of study and label-change requirements. PDUFA IV also eliminated calendar and time limitations on postapproval activities.

¹⁷ In addition to adding the new Section 736B to the FFDCA, PDUFA IV added a new Section 736A, authorizing the Secretary to collect fees related to the advisory review of prescription drug television advertising. This fee program was not implemented because the appropriators did not include it in the appropriations legislation; see CRS Report R40590, (continued...)

section, which also codified the requirements for annual performance and fiscal reports¹⁸ that had appeared in every PDUFA version, appears in **Table A-2** in **Appendix A**.

Table B-1 in **Appendix B** describes the commitments in the Agreement between FDA and industry representatives for PDUFA V. It also provides selected comments on differences between the PDUFA IV letter and the PDUFA V letter.¹⁹

PDUFA Impact on FDA Review Time and Budget

Review Time

The approval times for drugs and biologics applications provide a measure of PDUFA's effectiveness in meeting its primary goal: reducing the time between a manufacturer's submission of an NDA and FDA's approval decision. FDA and industry analysts have presented review time data in various ways—such as looking at all applications or distinguishing between standard and priority review.²⁰ **Figure 2**, for example, shows the median approval times of new molecular and biologic entities; these applications are important because they involve either “significant advances” in treatment or are “the first drugs approved in their therapeutic class.”²¹

A December 2011 FDA presentation indicated that, as of September 30, 2011, the agency data indicated that FDA had met or exceeded 10 of the 12 specified performance goals for applications submitted in FY2010 and were, thus far in FY2011, meeting or exceeding 11 of the 12 performance goals for FY2011 submissions.²²

(...continued)

Direct-to-Consumer Advertising of Prescription Drugs, by Susan Thaul.

¹⁸ FDA posts the annual PDUFA performance and fiscal reports at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/default.htm> and <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/PDUFA/default.htm>.

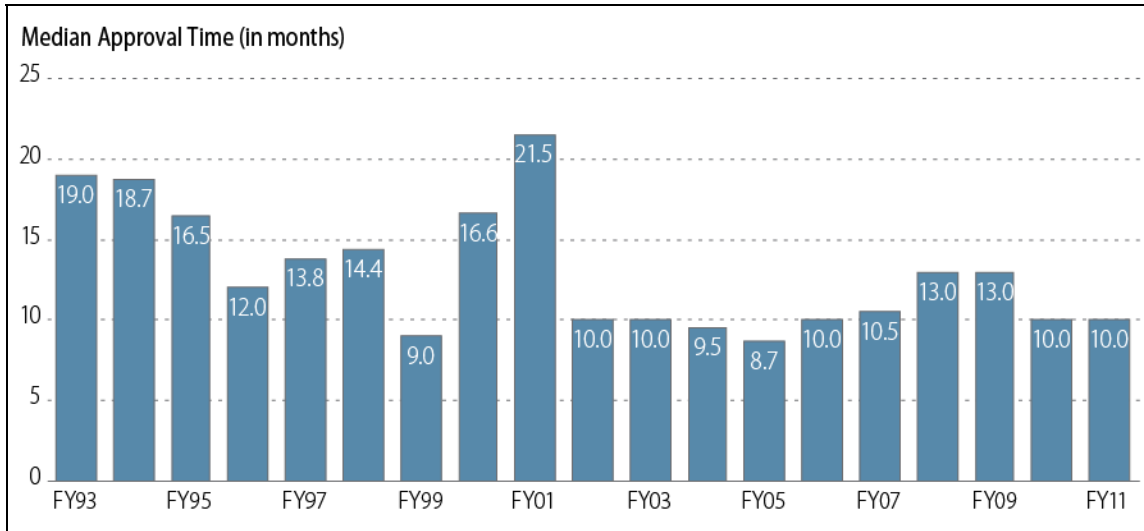
¹⁹ Food and Drug Administration (FDA), “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2012 through 2017,” January 13, 2012, <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>; and FDA, “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012,” <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119243.htm>.

²⁰ For a description of priority review, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by Susan Thaul.

²¹ John K. Jenkins, Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA. “CDER New Drug Review: 2011 Update,” presentation at FDA/CMS Summit, December 8, 2011, slide 14, <http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm282984.pdf>.

²² John K. Jenkins, Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA. “CDER New Drug Review: 2011 Update,” presentation at FDA/CMS Summit, December 8, 2011, slides 5 and 6, <http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm282984.pdf>. Performance goals (which are described later in this report in section titled “Industry-FDA Performance Goals and Procedures for PDUFA V: The Agreement”) include both a goal (e.g., review standard NDAs/BLAs in 10 months) and a performance measure (e.g., review in 10 months for 90% of standard NDAs/BLAs). The Agreement sets a goal for each type of submission.

Figure 2. Median Approval Times, New Molecular Entities (NMEs) and New Biologic Entities (NBEs), by Fiscal Year of Receipt



Source: FDA Center for Drug Evaluation and Research (CDER) data as of November 30, 2011, from John K. Jenkins, Director, Office of New Drugs, CDER, FDA. “CDER New Drug Review: 2011 Update,” presentation at FDA/CMS Summit, December 8, 2011, slide 18, <http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm282984.pdf>.

Notes: In its FY2002 PDUFA performance report to Congress, FDA commented on the spike in approval times “during the last few years of PDUFA II,” citing an “imbalance between resources and workload [that] resulted in significant stress to the program” (<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/UCM135621.pdf>, page 6 [PDF page 10]).

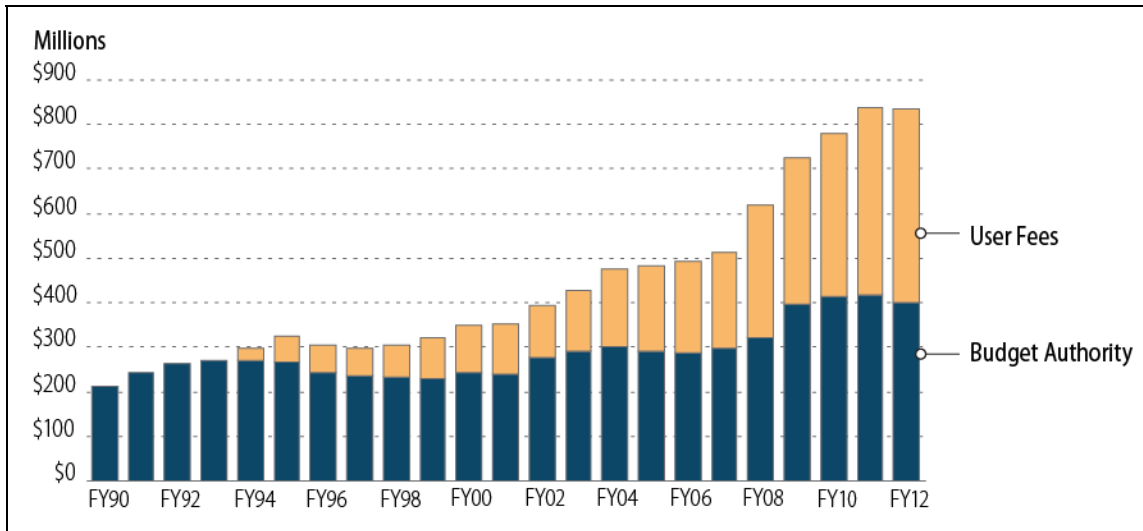
The FDA slide notes, for FY2007 through FY2011, that “Estimated median approval times. These figures are based on NME approvals to date, elapsed time of NMEs in process, and the historic approval rate of 75-80% of NMEs filed in a given year eventually gain FDA approval.”

Budget

Figure 3 presents the total program level for FDA’s Human Drug Program for each year from FY1990 to FY2012, with dollars adjusted for inflation to show the budgets’ usefulness across years. Beginning in FY1994, when prescription drug user fee revenue became part of the total budget, Figure 3 shows the separate contributions of budget authority²³ and user fee revenue to the total program level.

²³ FDA uses the term *budget authority* for only direct congressional appropriations.

Figure 3. FDA Human Drugs Program Budget, by Funding Source, for FY1990 through FY2012
(Adjusted to 2005 dollars)



Sources: FDA Justification of Estimates for Appropriations Committees documents, FY1992 through FY2012, and P.L. 112-55, the Consolidated and Further Continuing Appropriations Act, 2012 (Division A—Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, 2012).

Data have been adjusted for inflation to constant FY2005 dollars using “Total Non-defense” deflators from Office of Management and Budget, *Fiscal Year 2012 Historical Tables, Budget of the U.S. Government*, “Table 10.1, Gross Domestic Product and Deflators Used in the Historical Tables: 1940-2016,” pp. 211-212.

Notes: Total Program Level = Budget Authority + User Fees.

Table 1 shows, for the Human Drugs total program level, the relative contributions of the two funding sources—budget authority and user fees—over time. In the first year of PDUFA contributions to the FDA budget, the fee revenue accounted for 9.7% of the Human Drugs Program total program level. For FY2012, fees provide 51.8% of the total.

Table 1. FDA Human Drugs Program, Fees as a Percentage of Total Program Level for Selected Fiscal Years
(Unadjusted dollars)

Fiscal Year ^a	Budget Authority	PDUFA Fees	Total Program Level	
	\$ in millions	\$ in millions	Fees as % of Total Program Level	\$ in millions
1994	\$214.9	\$23.1	9.7%	\$238.0
1998	\$199.6	\$63.1	24.0%	\$262.6
2003	\$274.1	\$129.8	32.1%	\$403.8
2008	\$353.9	\$327.0	48.0%	\$680.9
2013	\$477.8	\$778.8	62.0%	\$1,256.6

Sources: FDA Justification of Estimates for Appropriations Committees documents, FY1996 through FY2010; and FDA Operating Plan for FY2013, prepared by the HHS Budget Office in response to Sec. 116 of the Continuing Resolution (CR) through March 27, 2013, provided to CRS November 15, 2012, CR Base FY2013 Annualized CR, excluding the 0.612% increase.

a. FY1994 was the first year that PDUFA revenue was reflected in the FDA budget. FY1998, FY2003, FY2008, and FY2013 were the first fiscal years of PDUFA II, III, IV, and V.

PDUFA V Package

PDUFA V consists of two parts: (1) statutory language that reauthorizes the program and (2) the performance goals and procedures agreement between FDA and industry, which this report refers to as the Agreement.²⁴ There are few differences between PDUFA IV and PDUFA V statutory language. The differences between the PDUFA IV and PDUFA V Agreements reflect the kinds of incremental changes and fine tuning that have occurred at each reauthorization. As described below, the changes address both communication and timing concerns about the review process, and support of a broader range of FDA activities to continue the development and use of regulatory science “[t]o enhance communications between FDA and sponsors during drug development and to meet the challenges of emerging science.”²⁵ As discussed below, tables in **Appendix A** relate to statutory language and tables in **Appendix B** relate to the FDA–industry Agreement.

Statutory Language

In describing PDUFA in current law (reflecting PDUFA V in FDASIA), this report refers to **Appendix A** for detail. **Table A-1** shows current law, noting where the PDUFA V statutory language for FDCA Section 736 differed from PDUFA IV. (**Table A-2** describes procedural steps outlined in FDCA Section 736B, which PDUFA V did not change.)

PDUFA V sets total PDUFA fee revenue for FY2013 at \$693 million, a 1.2% decrease from the \$702 million in PDUFA fees in the FY2012 budget.²⁶ PDUFA V modified the formulas for calculating inflation and workload adjustments in FY2014 through FY2017, and made technical changes in dates payable and collection procedures.

PDUFA V omitted several provisions that Congress had added to PDUFA IV. First, PDUFA IV had added \$225 million over the five-year authorization for postmarket safety activities. These additional fees are not explicitly mentioned in PDUFA V. Second, PDUFA I and all its reauthorizations have required what FDA and industry have called triggers: In order to collect and use PDUFA fees, Congress must maintain the levels of appropriated budget authority, adjusted for inflation, committed to both the review of human drug applications and to FDA overall. PDUFA IV had added a reverse trigger for FY2009 and FY2010: if appropriations had exceeded the amounts appropriated for FY2008, PDUFA IV would have allowed a reduction in PDUFA fee revenue. PDUFA V does not include the reverse trigger language.

PDUFA V includes a requirement for sponsors to submit NDAs and BLAs electronically. The requirement, a new FDCA Section 745A, is to begin no earlier than two years after the Secretary issues final guidance on electronic format standards, waivers, and exemptions, and a timetable.

²⁴ This document is referred to, at times, as the Agreement, the goals document, or the Commitment Letter.

²⁵ FDA, “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017,” draft posted September 1, 2011, transmitted to Congress January 13, 2012, <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>.

²⁶ PDUFA IV set PDUFA fee revenue at \$383 million for FY2008 to be adjusted annually for inflation and workload. PDUFA IV also added \$225 million over the five-year authorization for postmarket safety activities.

Industry-FDA Performance Goals and Procedures for PDUFA V: The Agreement

As directed by FFDCA Sec. 736B(d), FDA held regular meetings with industry representatives to negotiate commitments the agency would make regarding performance goals and procedures that the user fee revenue would support.²⁷ FDA also held required meetings with other stakeholders (including academic experts, and representatives of patient and consumer advocacy groups) and held a public meeting to obtain comments before completing the Agreement.²⁸ Items new to the PDUFA V Agreement fit into several general areas: (1) drug review performance goals, communication, and timing; (2) regulatory science; (3) risk-benefit assessment in decision-making; (4) drug safety; and (5) information technology and performance management. **Table B-1 in Appendix B** summarizes the elements in the performance goals letter, the Agreement, noting changes from the PDUFA IV letter where appropriate. The following paragraphs present highlights of those commitments.

Drug review performance goals, communication, and timing. At the core of PDUFA's history is FDA's commitment to completing review within a specified timeframe in exchange for an industry source of revenue to support that activity. Although subsequent PDUFA laws have added other kinds of commitments, the review time goals continue to be a focus of PDUFA Agreement negotiations. The PDUFA IV Agreement for NDAs specified that FDA would review and act on 90% of standard submissions within 10 months of receipt of the application and on 90% of priority submissions within 6 months of receipt; these continue in PDUFA V. The PDUFA V Agreement modified those goals for all original biologics license applications (BLAs) and for the subset of NDAs that involve new molecular entities (NMEs): it adds another 60 days, by specifying that the clock (toward the 10 or 6 month goals) begins 60 days after the receipt of those applications.

The PDUFA V Agreement establishes a new review model called "the Program" to "promote greater transparency and improve communication between the FDA review team and the applicant." It specifies circumstances under which FDA may extend the review time clock, new reporting requirements, procedures for agency response to applicants' questions on protocol design, and timeframes and requirements for certain meetings with applicants.

Regulatory science. The PDUFA V Agreement describes five areas in which FDA will use PDUFA revenue to enhance regulatory science to expedite drug development. Specific activities relate to enhanced communication with sponsors, developing meta-analysis methodologies, advancing the use of biomarkers and pharmacogenomics in drug review, advancing the development of patient-reported outcomes, and advancing the development of drugs for rare diseases.

²⁷ Minutes of the 38 meetings of FDA and industry representative from July 1, 2010, through May 17, 2011, are available on the FDA website (FDA, "PDUFA Meetings," <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm117890.htm>; webpage includes links to meeting minutes at "Industry Discussions on PDUFA V Reauthorization").

²⁸ The FDA website on PDUFA Meetings (FDA, "PDUFA Meetings," <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm117890.htm>) has minutes of the nine meetings of FDA and stakeholders from July 1, 2010, through March 18, 2011 (link to "Stakeholder Discussions on PDUFA V Reauthorization"), and the public meeting announcement, agenda, and transcript (link to "PDUFA Public Meeting October 24, 2011").

Risk-benefit assessment in decision-making. The PDUFA V Agreement says FDA will plan and begin to develop a “structured benefit/risk assessment in the new drug approval process.” The Agreement also says the agency will develop a process to obtain patient perspectives on risks and benefits.

Drug safety. The PDUFA V Agreement calls on FDA to evaluate Risk Evaluation and Mitigation Strategy (REMS) requirements that FDAAA added in 2007,²⁹ as well as working toward standardizing REMS for classes of drugs and integrating the REMS process into the health care system. The Agreement also includes activities around the Sentinel Initiative,³⁰ other pharmacovigilance systems, and related information systems and infrastructure.

Information technology and performance management. The PDUFA V Agreement includes items on required electronic submissions; data standardization; investments in automated, standards-based information technology; and improved FDA performance management.

Across all these areas, the PDUFA V Agreement specifies FDA commitments to produce draft and final guidance documents and to hold public meetings and workshops. These items are shown in **Table B-2** in **Appendix B**.

PDUFA Reauthorization as Driver of FDA Legislation

The five-year authority pattern that Congress first set with PDUFA I in 1992 has created a legislative vehicle that, every five years, attracts additional provisions—some closely related to user fee activities and others peripherally so. The urgency to pass PDUFA reauthorization stems from PDUFA revenue’s accounting for more than half the FDA Human Drugs Program budget.

In 2012, again, Congress built a multi-titled bill, the first of which was the Prescription Drug User Fee Amendments. The overall vehicle, FDASIA, included 10 other titles. A separate CRS report describes provisions in those titles, which cover reauthorization of the medical device user fee act, new user fee authorization for generic drug and biosimilar biological products, and provisions concerning pediatric drug development and labeling, medical device regulation, pharmaceutical supply chain security, antimicrobial development incentives, expedited drug approval, drug shortages, and other topics.³¹

²⁹ FDAAA expanded the risk management authority of FDA and organized several continuing and new elements into a new Risk Evaluation and Mitigation Strategy (REMS) process, which gave FDA the authority for structured follow-through, dispute resolution, and enforcement. FDA may require a REMS under specified conditions—including if it determines such a strategy is necessary to ensure that the benefits of a drug outweigh its risks. In addition to specific manufacturer-developed patient- and clinician-focused information, a REMS could require elements to assure safe use (ETASU). An ETASU is a restriction on distribution or use that is intended to (1) allow access to those who could benefit from the drug while minimizing their risk of adverse events and (2) block access to those for whom the potential harm would outweigh potential benefit. Such restrictions could define which health care providers, pharmacies, or health care settings could prescribe or dispense a drug, as well as patient-level monitoring or registry enrollment.

³⁰ FDA launched the Sentinel Initiative in 2008 to incorporate requirements of FDAAA for an active surveillance system to monitor safety and effectiveness of drugs once they are on the market. Through Sentinel, FDA plans to build a system of automated healthcare data from many sources (FDA, “FDA’s Sentinel Initiative,” <http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm>).

³¹ CRS Report R42680, *The Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144)*, coordinated by Susan Thaul.

Appendix A. Provisions in FFDCA Sections 735, 736, and 736B

Table A-I. Provisions in Sections 735 and 736 of the Federal Food, Drug, and Cosmetic Act Relating to Prescription Drug User Fees: Definitions and Authority to Assess and Use Drug Fees

Main Issue	Current Law (reflecting PDUFA V) ^a
FFDCA Sec. 735 [21 USC 379g]. Fees Relating to Drugs: Definitions.	
Definitions	<p>This section defines how several terms are used in this part: human drug application, supplement, prescription drug product, final dosage form, prescription drug establishment, process for the review of human drug applications, costs of resources allocated for the process for the review of human drug applications, adjustment factor, person, active, and affiliate.</p> <p>In particular, it defines the term “process for the review of human drug applications” as activities necessary for the review of human drug applications and supplements; the issuance of action letters; inspection of prescription drug establishments and other facilities; activities necessary for the review of applications for licensure of biological product establishments and for the release of lots of biologics; monitoring of research conducted in connection with the review of human drug applications; and postmarket safety activities, including adverse event data collection systems and development of analytical tools, and enforcement of study and label-change requirements.</p> <p>The term “costs of resources allocated for the process for the review of human drug applications” is defined as expenses and costs for FDA officers, employees, contractors, and advisory committees; information management; computer resources; facilities, furniture, equipment, materials and supplies; and collecting user fees and accounting for resources.</p>
FFDCA Sec. 736 [21 USC 379h]. Fees Relating to Drugs: Authority to Assess and Use Drug Fees.	
(a) Types of fees	There are three types of fees—application, establishment, and product—and certain exceptions.
(a)(1) Human drug application and supplement fee	<p>A human drug <i>application fee</i> is assessed for an application for which clinical data with respect to safety or effectiveness are required for approval. The fee for an application that does not require clinical data or for a supplement is half the application fee. The fee is due at the time of application or supplement submission.</p> <p>Exceptions are made for a previously filed application or supplement under certain conditions and for a designated orphan drug or indication.</p>
(a)(2) Prescription drug establishment fee	A prescription drug <i>establishment fee</i> is assessed annually for each establishment listed as manufacturing the prescription drug product named in an approved human drug application. Exceptions apply to certain compounded positron emission tomography (PET) drugs and designated orphan products.
(a)(3) Prescription drug product fee	A prescription drug <i>product fee</i> is assessed annually for each prescription drug product named in an application (except for a product whose manufacturer has had no pending application since September 1992). Exceptions apply to orphan drugs.
(b)(1,2) Fee revenue amounts	The law established total prescription drug user fee revenues for each fiscal year, subject to specified adjustments. It requires that each fee type provide one-third of the total revenue. Total fee revenue for FY2013 was set at \$693,099,000.
(b)(3)	PDUFA V changed the formula for the workload and inflation adjustment factors.

Main Issue	Current Law (reflecting PDUFA V) ^a
(c)(1) Inflation adjustment	<p>PDUFA V modified the inflation adjustment formula to be a weighted average of the CPI figure and FDA personnel cost figures, such that it is the sum of one plus—</p> <p>The CPI figure such that</p> <ul style="list-style-type: none"> —the average annual change for the first 3 years of the preceding 4 years of available data; and —multiplied by the proportion of all costs other than personnel compensation and benefits costs to total costs of the process for the review of human drug applications (as defined in FFDCa Section 735(6)) for the first 3 years of the preceding 4 fiscal years. <p>Calculates the FDA personnel cost such that it uses the first 3 of the preceding 4 fiscal years; multiplied by the proportion of personnel compensation and benefits costs to total costs of the process for the review of human drug applications for the first 3 years of the preceding 4 years.</p> <p>The adjustment is to be compounded to the sum of all adjustments made each fiscal year.</p>
(c)(2) Workload adjustment	<p>Fee revenues are adjusted to reflect changes in FDA's workload for the process for the review of human drug applications. The calculation was based on a weighted average of the change in the total number of human drug applications, commercial investigational new drug (IND) applications, efficacy supplements, and manufacturing supplements submitted. PDUFA IV added that</p> <ul style="list-style-type: none"> (1) the calculation count commercial IND applications as the number that were active during the preceding year; (2) the number of human drug applications is adjusted for changes in review activities. The adjustment may not result in fee revenues that are less than the totals established in (b) as adjusted for inflation; and (3) the Secretary must contract with an independent accounting or consulting firm to conduct periodic reviews and publish reports on the adequacy of the adjustment, including recommendations for change. The Secretary, after getting public comments, could change the methodology to be in effect the following fiscal year.
(c)(3) Final year adjustment	<p>The Secretary may <i>increase</i> total fee revenue if necessary to provide for up to three months of operating reserves for the process of human drug application review for the first three months following sunset.</p>
(c)(4) Annual fee setting	<p>The Secretary shall establish fees each year, 60 days before the start of each fiscal year.</p>
(c)(5) Limit	<p>For each fiscal year, the total amount of fees, as adjusted, may not exceed the total costs for the resources allocated for the process the review of human drug applications.</p>
(d) Fee waiver or reduction	<p>The Secretary must grant a waiver or reduction of fees if necessary to protect the public health, if the fee would be a significant barrier to innovation, if the fee would exceed the cost of the process of review, or if the applicant is a small business that is submitting its first human drug application. In deciding whether to grant a waiver or reduction, the Secretary may consider only the circumstances and assets of the applicant and any affiliate of the applicant.</p> <p>A small business is an entity with fewer than 500 employees, including employees of affiliates. Regarding waivers and reductions of fees, a small business is one that does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce.</p>
(e) Effect of failure to pay fees	<p>A human drug application or supplement that is not accompanied by the appropriate fee shall be considered incomplete; the Secretary shall not accept it for filing until all fees have been paid.</p>
(f) Limitations	<p>Fees shall be refunded for a fiscal year unless appropriations for FDA salaries and expenses are equal to or greater than the appropriations (excluding fees) for FY1997, adjusted.</p>

Main Issue	Current Law (reflecting PDUFA V) ^a
(g) Crediting and availability of fees	<p>Each five-year authorization specifies the amount of prescription drug user fees authorized to be appropriated for each fiscal year, subject to specified adjustments.</p> <p>The amount of fees collected in excess of the amount specified in appropriations acts is to be (1) credited to FDA's appropriation account, and (2) subtracted from the amount that would otherwise have been authorized to be collected during subsequent fiscal years. PDUFA IV specified that the amount of excess collections is based on a cumulative calculation of fees collected in each year, and that the offset must be reflected in the amount authorized to be collected in the final year.</p> <p>PDUFA V added a provision allowing the Secretary to accept early payment of authorized fees.</p>
(h) Collection of unpaid fees	Any unpaid fee shall be treated as a claim of the United States Government.
(i) Written requests for waivers, reductions, and refunds	A sponsor must submit a written request to the Secretary for any waiver, reduction, or refund not later than 180 days after the fee is due.
(j) Construction	"This section may not be construed to require that" HHS reduce FTE positions of officers, employees, and advisory committee members in other areas to offset those "engaged in the process of the review of human drug applications."
(k) Orphan drugs	An orphan drug, designated under FFDCA Section 526, is exempt from product and establishment fees under specified conditions if the drug is owned or licensed and is marketed by a company whose previous year gross worldwide revenue was less than \$50 million.

Sources: FFDCA §736 (21 U.S.C. §379h).

Note: Paragraph and subparagraph labeling follows current law (reflecting any changes made by FDASIA).

- a. Several provisions that PDUFA IV had added to the FFDCA were not included in PDUFA V. These were
 - (1) PDUFA IV had directed that, in addition to the adjusted revenue value based on \$392,783,000, there be fee revenues collected and used for drug safety in specific amounts summing to \$225 million from FY2008 through FY2012;
 - (2) PDUFA IV directed the Secretary to decrease (up to \$11.7 million) the fee revenue total if actual costs paid for rent and rent-related expenses are less than estimates made for such year in FY2006; and
 - (3) PDUFA IV added that the final year adjustment may decrease fee revenue if FY2009 or FY2010 appropriations for both FDA and the review of human drug applications exceed the amounts appropriated for those activities for FY2008—a "reverse trigger." This decrease was limited to a maximum of \$65 million.

Table A-2. Provisions in Section 736B of the Federal Food, Drug, and Cosmetic Act Relating to Prescription Drug User Fees: Reauthorization; Reporting Requirements

Main Issue	Current Law (reflecting PDUFA V)
Annual performance and fiscal reports	<p>The Secretary must submit annual fiscal and performance reports to Congress. Previous PDUFA legislation required the reports but did not direct that the provision become part of USC Title 21. FDAAA codified this provision.</p> <p>The Secretary must make publicly available on the FDA website the annual performance and fiscal reports to congressional committees.</p>
Consultation, public input, minutes of negotiation meetings, public availability	<p>The Secretary must, in preparation for the next PDUFA reauthorization, consult with congressional committees, scientific and academic experts, health-care professionals, representatives of patient and consumer advocacy groups, and the regulated industry to develop recommendations for PDUFA V, including goals and plans for meeting the goals.</p> <p>A public hearing and review of the Secretary's recommendations must be held following its negotiations with the industry, and the Secretary must include with the submission to Congress a summary of the public comments and changes made to the recommendations in response to them.</p> <p>Before presenting recommendations to Congress, the Secretary must make publicly available on the FDA website the minutes of all agency negotiation meetings with the regulated industry, including summaries of any substantive proposals made by any negotiating party and any significant controversies or differences of opinions and their resolution.</p>
Transmittal letter	<p>The Secretary is required to submit to congressional committees letters that propose performance goals and user fee amounts for the next round of PDUFA reauthorization legislation. The letter regarding PDUFA VI recommendations is due by January 15, 2017.</p>

Sources: FDCA §736B (21 U.S.C. §379h-2).

Appendix B. PDUFA V Agreement: Performance Goals and Procedures

**Table B-1. Performance Goals and Procedures in Agreement
Between FDA and Industry Representatives for FY2013 through FY2017
Under PDUFA V**

Topic	PDUFA V commitments
I. Review performance goals	<p>For major types of applications and efficacy and manufacturing supplements, states (1) the time in which FDA agrees to review and act on an application, and (2) the percentage of applications for which FDA agrees to meet that goal.</p> <p>Goals for new drug applications (NDA) and biologics license applications (BLA) vary based on whether the application involves a new molecular entity (NME) or the class of a resubmitted application, and whether FDA considers the application as standard or priority.</p> <p>For example, for non-NME original NDAs, FDA agrees to review and act on 90% of standard submissions within 10 months of receipt; and on 90% of priority submissions within 6 months of receipt.</p>
II. New molecular entity NDA and original BLA performance goals	<p>For NME NDAs and original BLAs, FDA agrees to review and act on 90% of standard submissions within 10 months of the 60 day filing date, and on 90% of priority submissions within 6 months of the 60 day filing date. [Note: PDUFA V added 60 days to the review time for NME NDAs and original BLAs by starting the clock (toward the 10-month and 6-month goals) 60 days after the filing date rather than on the filing date.]</p> <p>PDUFA V established a new review model called “the Program” to “promote greater transparency and improve communication between the FDA review team and the applicant.” Elements include a pre-submission meeting, original application submission, a “Day 74 Letter,” review performance goals, mid-cycle communication, “Discipline Review Letters,” late-cycle meeting, inspections, and a quality system. Includes a continuous evaluation of the Program by an independent contractor, with details specified in the Agreement.</p>
III. First cycle review performance	<p>Notification of issues: Within 74 calendar days after FDA receives the original submission, the agency will tell the applicant the substantive review issues it identified during the initial filing review, including if there were no substantive issues identified. The filing review is preliminary and “is not indicative of deficiencies that may be identified later in the review cycle.”</p> <p>Notification of planned review timelines. Also within 74 days, FDA will provide its planned timeline for review of the application, which is subject to requirements specified in the Agreement.</p> <p>PDUFA V added: When the review division agrees to review an applicant-submitted major amendment and the initial planned review timeline is no longer applicable, FDA may extend the review clock. Except in rare circumstances, such extension would “be limited to occasions where review of the new information could address outstanding deficiencies in the application and lead to approval in the current review cycle.”</p> <p>In its annual PDUFA performance report, FDA will report on its performance in including a planned review timeline along with the notification of issues identified during filing review. The Agreement provides reporting details.</p>
IV. Review of proprietary names to reduce medication errors	<p>FDA will review proprietary names submitted during the IND phase and along with the NDA/BLA according to timeframes detailed in the Agreement.</p>

Topic	PDUFA V commitments
V. Major dispute resolution	For disputes over procedural or scientific matters that cannot be resolved at “signatory authority level,” the Agreement allows for written appeals to the next level, according to specified criteria. FDA agrees to respond to 90% of such appeals within 30 days of their receipt.
VI. Clinical holds	After a sponsor submits a complete response to a clinical hold, FDA agrees to respond to 90% of such responses within 30 days of receipt.
VII. Special protocol question assessment and agreement	The Agreement lays out procedures, including timing, and criteria for sponsor submissions of a limited number of specific questions about protocol design and regulatory and scientific requirements. FDA agrees to complete and return 90% of these special protocol assessments and agreement requests within timeframes, and to track and report the number of such assessments and resubmissions per original special protocol assessment.
VIII. Meeting management goals	<p>Regarding requests for specific types of meetings (Types A, B, C, and pre-IND), the Agreement outlines timeframes and notification requirements for requests and meeting schedules, content, attendees, documentation, and minutes.</p> <p>“FDA shall publish revised draft guidance on formal meetings between FDA and sponsors no later than the end of FY2013.”</p> <p>The PDUFA V Agreement adds criteria for when FDA or the sponsor could provide a written response to questions rather than hold a meeting. It also specifies how to categorize meetings (e.g., Type A or Type B) that address REMS and other postmarketing requirements or post-action meetings. The Agreement adds the draft guidance requirement.</p>

Topic	PDUFA V commitments
IX. Enhancing regulatory science and expediting drug development	<p>The PDUFA V Agreement includes this new section.</p> <p>(1) Promoting innovation through enhanced communication between FDA sponsors during drug development. FDA will develop a “dedicated drug development communication and training staff,” train staff, increase sponsor liaison, and publish draft guidance by the end of the second quarter of FY2015.</p> <p>(2) Advancing the science of meta-analysis methodologies. FDA will develop a dedicated expert review team “to explore the practical application of scientific approaches and best practices, including methodological limitations, for the conduct of meta-analyses in the context of FDA’s regulatory review process”; hold a public meeting; publish a draft guidance to “promote a better understanding and more consistency among Agency, industry, and other stakeholders regarding meta-analyses and their role in regulatory decision-making”; and complete final guidance.</p> <p>(3) Advancing the use of biomarkers and pharmacogenomics. FDA will “develop staff capacity to review submissions that contain complex issues involving pharmacogenomics and biomarkers”; provide training for FDA staff; and “hold a public meeting to discuss the current status of biomarkers and pharmacogenomics and potential strategies to facilitate scientific exchanges in regulatory and non-regulatory contexts.”</p> <p>(4) Advancing development of patient-reported outcomes (PROs) and other endpoint assessment tools. FDA will “develop clinical and statistical staff capacity ... advance the development of these tools ... focus on review and qualification of endpoint assessment tools”; and “hold a public meeting to discuss FDA’s qualification standards for drug development tools, new measurement theory, and implications for multi-national trials.”</p> <p>(5) Advancing development of drugs for rare diseases. FDA will plan for the CDER Rare Disease Program (RDP), increase its staff, and fill the CBER Rare Disease liaison position. The CDER and CBER RDPs will “develop and disseminate guidance and policy related to advancing and facilitating the development of drugs and biologics for rare diseases,” including improving FDA reviewer understanding, considering nontraditional clinical development, design, endpoints, and statistical analysis; and encouraging flexibility and scientific judgment. FDA will hold a public meeting, train staff, emphasizes “the role of the RDP staff as members of the review team ...”; and “develop an evaluation tool to evaluate the success of the activities of the RDP.... ”</p>
X. Enhancing benefit-risk assessment in regulatory decision-making	<p>The PDUFA V Agreement includes this new section.</p> <p>FDA “will develop a five-year plan to further develop and implement a structured benefit/risk assessment in the new drug approval process”; publish draft plan for public comment; begin to implement the framework “across review divisions in the pre-and post-market human drug review process;” update the plan as needed and post all updates on the FDA website. The Agreement outlines plan components to include two public workshops, an evaluation plan, and revision as appropriate of FDA templates and Manuals of Policies and Procedures.</p> <p>FDA will “initiate a public process to nominate a set of disease areas that could benefit from a more systematic and expansive approach to obtaining the patient perspective on disease severity or unmet medical need” to include four meetings per year; “increase utilization of FDA’s Patient Representatives”; and train staff and “fully integrate structured benefit/risk assessment into the regulatory review process.”</p>

Topic	PDUFA V commitments
XI. Enhancement and modernization of the FDA drug safety system	<p>The PDUFA V Agreement includes this new section.</p> <p>(1) Measure the effectiveness of REMS and standardize and better integrate REMS into the healthcare system. FDA will “continue to develop techniques to standardize REMS and with stakeholder input seek to integrate them into the existing and evolving (e.g., increasing electronic) healthcare system”; “develop and issue guidance”; hold public meetings and public workshops; and issue guidance on “methodologies for determining whether a specific REMS with elements to assure safe use (ETASU) is (i) commensurate with the specific serious risk listed in the labeling of the drug and (ii) considering the observed risk, not unduly burdensome on patient access to the drug.”</p> <p>(2) Sentinel as a tool for evaluating drug safety issues that may require regulatory action. FDA will “hold or support public meetings” to get stakeholder comments on Sentinel projects; fund 4-6 activities “designed to further evaluate safety signals that ... have served as the basis for regulatory action(s) ... or ... to help determine the utility and validity of the Sentinel System to evaluate other types of signals in population-based datasets”; conduct or fund interim and final assessments “to evaluate the strengths, limitations and the appropriate use of Sentinel for informing regulatory actions (e.g., labeling changes PMRs and PMCs) to manage safety issues.”</p> <p>(3) Conduct and support activities designed to modernize the process of pharmacovigilance. FDA will continue to use expanded database resources, including population-based epidemiologic data, “to conduct targeted post-marketing surveillance, evaluate class effects of drugs, and potentially conduct signal detection ...”; train and develop staff; and develop needed information technology infrastructure.</p> <p>(4) Information systems and infrastructure. FDA will continue to work on its adverse event reporting system and surveillance tools, IT infrastructure, and workflow tracking system.</p>
XII. Improving the efficiency of human drug review through required electronic submissions and standardization of electronic drug application data	<p>The PDUFA V Agreement includes this new section.</p> <p>FDA will, according to details and a timetable in the Agreement, consult with stakeholders to issue draft and then final guidance on the standards and format of electronic submissions of applications. FDA will, with stakeholder input, develop standardized clinical and nonclinical data terminology and implementation guides.</p>
XIII. Progress reporting for PDUFA V and continuing PDUFA IV initiatives	<p>The PDUFA V Agreement includes this new section.</p> <p>FDA will report annually on its website on the progress of specified initiatives.</p>

Topic	PDUFA V commitments
XIV. Information technology goals	<p>“FDA is committed to achieve the long-term goal of improving the exchange, review, and management of human drug and biologic applications throughout the product life cycle through strategic investments in <i>automated, standards-based</i> information technology (IT).” FDA will post and update a five-year plan regarding IT investments; conduct annual assessments and updates; and meet quarterly with industry stakeholders.</p> <p>FDA will annually “measure and report progress toward achievement of objectives” including the number and percentages of the different types of FDA submissions received in valid electronic format.</p> <p>The PDUFA V Agreement added new reporting requirements.</p> <p>FDA will also annually measure and report regarding the number and significance of IT guidance issued requiring certain unanticipated industry submissions changes; and spending on IT systems regarding the review of human drug applications, both PDUFA- and other-funded.</p>
XV. Improving FDA performance management	<p>The Agreement outlines various studies to foster improved access to internal and external expertise; reviewer development; science and information management tools; inter- and intra-Center consistency, efficiency, and effectiveness; reporting of management objectives; accountability for use of user fee revenues; focused investment in the process of drug review; and communication between FDA and industry.</p> <p>Studies to be conducted by FDA or by independent contractors to include assessment of the impact of electronic submissions and data standards; assessments of the PDUFA review activity adjustment methodology; assessment of the Program for NME NDAs and original BLAs; assessment of the impact of the benefit-risk framework; and development of a tool to evaluate the Rare Disease Program. The PDUFA V Agreement added the latter three study requirements.</p>
XVI. Definitions and explanations of terms	<p>The Agreement defines the term “review and act on” to mean “the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.”</p> <p>It defines types of applications, including major amendments; Class 1 and Class 2 resubmitted applications; and Type A, Type B, and Type C meetings.</p> <p>The Agreement states that “performance goals and procedures also apply to original applications and supplements for human drugs initially marketed on an over-the-counter (OTC) basis through an NDA or switched from prescription to OTC status through an NDA or supplement.”</p> <p>It provides IT-specific definitions for program, standards-based, FDA standards, and product life cycle.</p>

Source: FDA, “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017,” draft posted September 1, 2011, transmitted to Congress January 13, 2012, <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>. Document is referred to, at times, as the Commitment Letter or the Agreement; and FDA, “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012,” <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119243.htm>.

Note: Topic numbering corresponds to the ordering in the PDUFA V Agreement; these are usually different from the PDUFA IV numbering.

Table B-2. FDA Commitments to Produce Guidance Documents and Hold Public Meetings and Workshops, FY2013-FY2017

General Topic	New Guidance	Public Meeting or Workshop
Drug review, performance goals, communication, and timing	<ul style="list-style-type: none"> • formal meetings between FDA and sponsors 	<ul style="list-style-type: none"> • stakeholders to comment on the success of the Program
Regulatory science	<ul style="list-style-type: none"> • best practices for communication between FDA and IND sponsors during drug development • FDA's intended approach to the use of meta-analyses in the FDA's regulatory review process • advancing and facilitating the development of rare disease products 	
Risk-benefit assessment in decision-making		<ul style="list-style-type: none"> • workshops on benefit-risk considerations from the regulator's perspective
Drug safety	<ul style="list-style-type: none"> • how to apply the statutory criteria to determine whether a REMS is necessary to ensure that the benefits of a drug outweigh the risks • methodologies for determining whether a specific REMS with elements to assure safe use (ETASU) is commensurate with risk ... and is not unduly burdensome on patient access 	<ul style="list-style-type: none"> • strategies to standardize REMS [Risk Evaluation and Mitigation Strategies], where appropriate, with the goal of reducing the burden of implementing REMS on practitioners, patients, and others in various healthcare settings • workshops on methodologies for assessing whether REMS are mitigating the risks they purport to mitigate and for assessing the effectiveness and impact of REMS • current and emerging Sentinel projects
Information technology and performance management.	<ul style="list-style-type: none"> • standards and format of electronic submissions of applications 	

Source: CRS array of information in FDA, "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017," draft posted September 1, 2011, transmitted to Congress January 13, 2012, <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>.

Author Contact Information

Susan Thaul
 Specialist in Drug Safety and Effectiveness
 sthaul@crs.loc.gov, 7-0562