FY 2006 PDUFA FINANCIAL REPORT

REQUIRED BY THE

PRESCRIPTION DRUG USER FEE ACT OF 1992

AS AMENDED BY THE

FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT OF 1997

AND BY THE

PRESCRIPTION DRUG USER FEE AMENDMENTS OF 2002

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

AUGUST 2007

THE SECRETARY DEPARTMENT OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

August 8, 2007

Honorable Richard Cheney
President of the Senate
United States Senate
Washington, D.C. 20510

Dear Mr. President:

The Prescription Drug User Fee Act of 1992 (PDUFA), as amended, requires an annual financial report to Congress. Please find enclosed the Fiscal Year 2006 report which documents how the Food and Drug Administration (FDA) met each of the necessary conditions specified in PDUFA for continued collection of prescription drug user fees. Availability of these fees makes FDA better able to strengthen its drug review process and meet the performance goals established for this program.

I look forward to working with the Congress during the reauthorization of PDUFA in the next few months.

Sincerely,

Michael O. Leavitt

Enclosure

Identical letters to:
Speaker of the House of Representatives
Chairman and Ranking Minority Member, Committee on Health, Education, Labor, and Pensions, United States Senate
Chairman and Ranking Minority Member, Committee on Energy and Commerce, House of Representatives

EXECUTIVE SUMMARY

The Prescription Drug User Fee Amendments of 2002 require the Food and Drug Administration (FDA or the agency) to report annually on the financial aspects of its implementation of the Prescription Drug User Fee Act (PDUFA), as amended. This report covers fiscal year (FY) 2006.

PDUFA specifies that the following three conditions must be satisfied each year in order for FDA to collect and spend PDUFA fees:

1. FDA's overall Salaries and Expenses Appropriation, excluding fees, must exceed FDA's overall FY 1997 salaries and expenses appropriation, excluding fees and adjusted for inflation.
2. Fee revenues collected must be specified in Appropriation Acts.
3. FDA must spend at least as much from appropriated funds for the review of human drug applications as it spent in FY 1997, adjusted for inflation, within certain tolerances.

This report describes how FDA met those specific statutory conditions or "triggers" during FY 2006. The statements and tables included in this report also provide the user fee revenues and expenditures in FY 2006, the carryover balance, and comparative data for earlier periods.

For FY 2006, FDA collected $316 million in fees, including fees collected for earlier periods. This is more than the $297 million FDA projected at the beginning of the year when fees for FY 2006 were established. The higher revenue is attributable to receiving a greater than anticipated number of fee-paying applications.

In FY 2006, FDA obligated $306 million from PDUFA fee revenues. This accounted for about 58 percent of all funds obligated by FDA from all sources in support of the process for the review of human drug applications. This $306 million was about $10 million less than net collections for the year, increasing the balance of funds collected and appropriated in previous years, and still available for obligation, to $76 million at the end of FY 2006. Over 60 percent of funds spent from all sources were for employee salaries and benefits, and the balance were for costs necessary to support and maintain those employees.

Challenges facing FDA in FY 2007 include hiring, training, and maintaining the staff to meet the PDUFA III goals and maintaining application review productivity. In addition, during the current fiscal year, FDA must work closely with the relevant congressional committees to support the enactment of reauthorization legislation for PDUFA before the current authorization expires on September 30, 2007.

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BACKGROUND

Enacted in 1992, PDUFA authorized FDA to collect fees from the pharmaceutical industry to be spent on drug review, in addition to minimum amounts that must continue to be spent from appropriations. FDA used these additional resources to hire and support additional staff for the review of human drug applications, so that safe and effective drug products would reach the American public more quickly. PDUFA was a very successful program. With the support of the pharmaceutical industry, other stakeholders, and the Administration, Congress amended and extended PDUFA in 1997 and again in 2002. The current program (PDUFA III) expires at the end of FY 2007.

Under PDUFA III, application fees, establishment fees, and product fees each contribute one third of the total fee revenues in a fiscal year. An application fee must be submitted when certain new drug applications (NDAs) or biologic license applications (BLAs) are submitted. Product and establishment fees are due annually on October 1. The total revenue amounts derived from each of the categories – application fees, product fees, and establishment fees – are set by the statute for each fiscal year. These statutory amounts must be adjusted for cumulative inflation since FY 2003, and for changes in drug review workload in each fiscal year. PDUFA III authorizes FDA to set user fees in each fiscal year, so that the total revenue that FDA receives from each fee category approximates the statutory amounts after the adjustments for inflation and the workload.

PDUFA III also requires FDA to submit two reports to Congress each fiscal year. A performance report is to be sent within 60 days after the end of a fiscal year, and a financial report is to be sent within 120 days. The FY 2006 PDUFA Performance Report, which discusses FDA's progress in meeting the goals referred in PDUFA III, is being transmitted separately to Congress. This report is FDA's FY 2006 PDUFA Financial Report, covering the period from October 1, 2005, to September 30, 2006.

As required by the statute, this report will present the legal conditions or "triggers" that must be satisfied before FDA can collect and spend the fees, and the calculations on how these conditions were met in FY 2006. This report also presents summary statements of FY 2006, earned revenue by fee source, and fee obligations by expense category. This report also presents the total costs, from both fee revenues and appropriation, of the process for the review of human drug applications, as defined in PDUFA III.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 2006

PDUFA III imposes three legal conditions or "triggers" that FDA must satisfy each year before the agency can collect and spend user fees. The calculations on how these conditions were met in FY 2006 are summarized below, and are explained in greater detail in Appendix A.

The **first condition** is that FDA's overall Salaries and Expenses Appropriation (excluding user fees) must meet or exceed FDA's overall FY 1997 Salaries and Expenses Appropriation (excluding user fees and adjusted for inflation). In FY 2006, FDA's overall Salaries and Expenses Appropriation (excluding user fees and excluding rent to the U.S. General Services Administration (GSA), which was also not included in the FY 1997 Appropriation amount) totaled $1,370,398,000. FDA's FY 1997 total Salaries and Expenses appropriation (excluding user fees) and adjusted as required by the statute, and rounded to the nearest thousand dollars, was $996,019,000. Therefore, since the FY 2006's amount is greater, the first condition was met.

The **second condition** is that the amount of user fees collected in each year must be specified in Appropriation Acts. The President signed the Appropriation Act (Public Law 109-97) specifying amounts collectable from fees during FY 2006, on November 10, 2005. It provided for $305,332,000 to come from prescription drug user fees. The Appropriation Act specified that the fees collected could remain available until expended. Thus, the second condition was met.

The **third condition** is that FDA may collect and spend user fees only in years when FDA also uses a specified minimum amount of appropriated funds for the review of human drug applications. The specified minimum is the amount FDA spent on the review of human drug applications from appropriations (exclusive of user fees) in FY 1997, adjusted for inflation. That amount, adjusted for inflation, is $179,726,634. In FY 2006, FDA obligated $218,659,212 from the appropriated funds for the review process of human drug applications. Since this amount exceeds the specified minimum amount, the third condition has been met.

Appendix A provides a more detailed calculation and explains how FDA met each of these three statutory conditions.

USER FEE REVENUES

PDUFA III specifies that FDA shall collect fee revenues from establishment, product, and application fees. The statute specifies revenue amounts for each of these categories and specifies that the statutory amounts are to be adjusted in each fiscal year for both inflation and workload. FDA then establishes fees at the beginning of each fiscal year so that the total revenue collected approximates the adjusted statutory total fee amount.

Under PDUFA, fees collected and appropriated, but not spent by the end of a fiscal year, continue to remain available for FDA to spend in future fiscal years. The balances carried over from year to year are described in the section on carryover balances beginning on page 6.

The following table provides a breakout of user fees collected by fee category during the past two fiscal years, and also reflects estimates of receivables.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE REVENUES BY FEE SOURCE
As of September 30, 2006

Fiscal Year	FY 2005	FY 2006
Fees Collected:		
Application Fees	$81,969,485	$104,388,192
Establishment Fees	$103,782,226	$103,258,983
Product Fees	$99,895,450	$92,600,810
TOTAL FEES COLLECTED:	**$278,647,161**	**$300,247,985**
Fee Receivables:		
Application Fees	$336,000	$383,700
Establishment Fees	$131,100	$274,434
Product Fees	$250,260	$337,040
TOTAL FEES RECEIVABLE:	**$717,360**	**$995,174**
Total User Fee Revenues:	**$286,364,521**	**$301,243,159**

Note that user fee revenues are reported in the year the fee was originally due—referred to as cohort years. For example, a fee due in FY 2005, even if it is received in FY 2006, is attributed to FY 2005 revenues. Totals reported for each year are net of any refunds for that year.

FDA bills the uncollected fees twice a year – August and November. In order to ensure the quality of the information provided in this financial report, FDA updates prior year numbers each year.

OBLIGATION OF USER FEE REVENUES

User fee revenues are expended only for costs necessary to support the process for the review of human drug applications, as defined in PDUFA III. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C. In FY 2006, FDA obligated $305,644,137 from user fee revenues.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
As of September 30, 2005 and 2006

Expense Category	FY 2005	FY 2006
Personnel Compensation and Benefits	$169,050,442	$188,550,842
Travel and Transportation	$3,866,739	$3,109,474
Rent	$11,212,000	$14,100,000
Communications	$2,059,157	$4,377,218
Contract Services	$66,343,864	$87,831,998
Equipment and Supplies	$15,849,032	$6,782,580
Other	$1,052,566	$892,025
TOTAL OBLIGATIONS:	**$269,433,800**	**$305,644,137**

FDA dedicated 1,277 staff-years to the review of human drug applications in FY 1992, before PDUFA was enacted. FDA conducted a time reporting study in 1993 to determine the percentage of time each organizational component devoted to user fee related activities. The data from this study allowed FDA to calculate the personnel-related costs of the drug review process. The percentages are updated regularly through additional time surveys, which parallel the method used by independent consultants in FY 1993. The report describes the development of the costs associated with the review of human drug applications in more detail in Appendix D.

In FY 2006, PDUFA fees and appropriations paid for 1,414 more staff-years than were used in FY 1992 for the review process of human drug applications. Employee salary and benefits paid from user fees in FY 2006 totaled about 62 percent of the obligations. This includes all pay and benefits for the additional personnel.

In May 2006, the FDA Electronic Submissions Gateway (ESG) went into production. FDA ESG is an FDA-wide solution that enables the secure submission of electronic regulatory submissions. It is the central transmission or single point of entry for sending PDUFA regulatory submissions electronically to FDA. The electronic submission process encompasses the receipt, acknowledgment of receipt (to the sender), routing, and notification (to a receiving Center or Office) of the delivery of an electronic submission. By the end of FY 2006, the ESG had received and processed over 33,000 pre-marketing and post-marketing submissions. Information on the ESG process and requirements is available at http://www.fda.gov/esg/. The FDA also enhanced the e-CTD (Electronic Common Technical Document) review system to provide reviewers with additional search capabilities and to track the progress of the e-CTD submission review at the section level. In FY 2006,

there was a dramatic increase in the number of e-CTD submissions with approximately 4,000 e-CTD submissions received. Since FY 2003 the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) have received over 5,000 e-CTD submissions. The e-CTD guidance and specifications are available at http://www.fda.gov/cder/regulatory/ersr/ectd.htm. Both of these major initiatives enabled the FDA to meet the electronic application and submission commitments under PDUFA that are designed to increase the number of electronic submissions and to provide FDA reviewers with an electronic standardized format for the review of PDUFA regulatory submissions.

FDA continues to make progress in the consolidation of information technology (IT) infrastructure through collaboration with the Department of Health and Human Services (HHS). In FY 2006, FDA moved over 2,000 CDER staff to the White Oak campus, migrated CDER staff to the HHS email environment, and consolidated the FDA extranet environment as part of the ESG project. FDA extranet is an infrastructure or system that FDA shares with external stakeholders using the internet. FDA continued to strengthen and improve IT project management capabilities to ensure that all IT projects follow standardized industry best practices. FDA has established project review guidelines, conducted stage gate reviews, conducted post-implementation lessons-learned sessions for each major IT investment, and requires earned value management reporting on all IT investments.

CARRYOVER BALANCES

Under PDUFA, fees collected and appropriated but not obligated by the end of a fiscal year continue to remain available to FDA in future fiscal years. These revenues are referred to as carryover balances. The net result of operations in FY 2006 increased the carryover balances by $9,858,648.

The table below captures the changes in carryover balances from FY 1993.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF COLLECTIONS, OBLIGATIONS, AND CARRYOVER BALANCES BY FISCAL YEAR
As of the end of each fiscal year shown, and not including payments for next fiscal year

Fiscal Year	Beginning Carryover	Net Collections	Obligations	Year-End Carryover
1993	-	$28,531,996	$8,949,000	$19,582,996
1994	$19,582,996	$53,730,244	$39,951,020	$33,362,220
1995	$33,362,220	$70,953,500	$74,064,015	$30,251,705
1996	$30,251,705	$82,318,400	$85,053,030	$27,517,075
1997	$27,517,075	$93,234,125	$84,289,046	$36,462,154
1998	$36,462,154	$132,671,143	$101,615,000	$67,518,297
1999	$67,518,297	$126,580,456	$122,515,000	$71,583,753
2000	$71,583,753	$133,060,339	$147,276,000	$57,368,092
2001	$57,368,092	$138,761,294	$160,713,000	$35,416,386
2002	$35,416,386	$149,078,939	$161,812,100	$22,683,225
2003	$22,683,224	$209,667,051	$200,154,500	$32,159,776
2004	$32,195,776	$251,617,821	$232,081,500	$51,732,097
2005	$51,732,097	$282,860,095	$269,433,800	$65,158,392
2006	$65,789,792	$315,502,786	$305,644,137	$75,648,440
2007	$75,648,440			

The balances above reflect cumulative cash at the beginning/end of each fiscal year, and the net cash collected during each fiscal year for all cohort years, but do not reflect any cash received for future fiscal year cohorts. The figures do not include accounts receivable. The net collections balance shown above for FY 2006 of $315,502,786 is greater than the FY 2006 collections balance on page 3 ($300,247,985). This is because the FY 2006 net collections figure also includes some prior years' receivables that FDA collected in FY 2006. In FY 2006, FDA made a correction to FY 2005 year-end carryover balance because of miscalculation. FDA kept FY 2005 year-end carryover as shown in last year's financial report ($65,158,392), and recorded the correct amount in FY 2006 beginning carryover balance ($65,789,792). There are also a number of claims on these carryover funds. These claims are explained below.

COLLECTION CEILINGS, POTENTIAL REFUNDS AND OFFSETS

PDUFA prohibited FDA from keeping fees in excess of the amount specified in appropriations (collection ceiling) each fiscal year through FY 1997. Amounts collected that exceed collection ceilings through FY 1997 were required to be refunded. A total of $6.3 million surplus collections from this period were refunded in FY 2000 and FY 2001.

Under PDUFA II and III, collections in excess of fee amounts appropriated after FY 1997 may be kept and used to reduce fees that would otherwise be assessed in a later fiscal year. The following table depicts the net collections, the collection ceilings specified in appropriations, and the amounts that FDA may either refund or use to offset future collections.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF FEES COLLECTED, COLLECTION CEILINGS, AND POTENTIAL REFUNDS
As of September 30, 2006

Fiscal Year	Collections Realized	Collection Ceiling	Potential Refund	Potential Offset to Future Collections
1993	$35,973,500	$36,000,000	-	
1994	$56,284,277	$56,284,000	$277	
1995	$77,498,800	$79,423,000	-	
1996	$84,726,488	$84,723,000	$3,488	
1997	$87,654,312	$87,528,000	$126,312	
1998	$117,849,016	$117,122,000		$727,016
1999	$125,729,367	$132,273,000		-
2000	$140,991,812	$145,434,000		-
2001	$138,421,429	$149,273,000		-
2002	$141,408,975	$161,716,000		-
2003	$218,302,684	$222,900,000		-
2004	$257,636,300	$249,825,000		$7,811,300
2005	$285,647,161	$284,394,000		$1,253,161
2006	$300,247,985	$305,332,000		
		Total:	**$130,077**	**$9,791,477**
Amount Offset When Fees for FY 2007 Were Determined				$7,957,922
Balance Remaining to be Offset in the Future				**$1,833,555**

RESERVE FOR REFUNDS AND OFFSET FOR FUTURE COLLECTIONS

The net collections exceeded the appropriations in FY 1994 ($277), FY 1996 ($3,488), and FY 1997 ($126,312), and could be potentially refunded. Further refunds of remaining pre-1998 balances will not be made until all pending appeals from this period are resolved. However, FDA must keep $130,077 in reserve until the agency resolves appeals or makes refunds.

FY 1998 collections exceeded the appropriations limit by $727,016. In FY 2004 collections exceeded the appropriation limit by $7,811,300 and in FY 2005 collections exceeded the appropriation limit by $1,253,161, for a total of $9,791,477 in excess collections. When FDA set fees for FY 2007 in August of 2006, the amount of fees established for FY 2007 was offset by $7,957,922 of collections in excess of appropriations. A total of $1,833,555 remains to be offset in a future year.

Some requests for refunds or waivers for these years are still pending. Until refund and waiver requests are settled, however, FDA will keep $2,000,000 in reserve as an offset for future refunds.

OTHER RESERVES AND BALANCE AVAILABLE FOR ALLOCATION

The table below provides a summary of carryover balances as of September 30, 2006, and anticipated claims on those balances. Included in those claims is also a requirement, from the agency's FY 2007 appropriation request, to spend $8,188,000 of the carryover funds to support consolidation into the new White Oak facility in FY 2007.

Due to a change in PDUFA III law requiring establishment and product fees to be paid for FY 2003 and subsequent years by the first of the fiscal year, FDA no longer needs to have a 3-month reserve for future operations at the end of each fiscal year—at least until the end of FY 2007. The carryover amount shown as available for allocation in the table below ($63,496,808) is enough to fund estimated FY 2007 operations for approximately 2½ months.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CARRYOVER BALANCE

As of September 30, 2006

Status of Carryover Funds	Amount
Reserve for Refunds	$2,130,077
Reserve for Future Collection Offset	$1,833,555
Reserve White Oak Consolidation in FY 2007	$8,188,000
Available for Allocation	$63,496,808
TOTAL Carryover Balance	$75,648,440

TOTAL COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS

The following table presents the costs for the review of human drug applications for FY 2005 and FY 2006 by organizational components. It indicates the full cost of the process for the review of human drug applications, including costs paid both from appropriations and from user fee revenues. The amounts are based upon the obligations recorded at the end of each fiscal year. In the past, over 81 percent of amounts obligated are expended within 1 year, and 96 percent within 2 years. Thus, obligations represent an accurate measure of costs.

FOOD AND DRUG ADMINISTRATION
PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS – TOTAL COSTS
As of September 30, 2006

FDA Component	FY 2005	FY 2006
Center for Drug Evaluation and Research (CDER)	$332,515,484	$363,449,183
Center for Biologics Evaluation and Research (CBER)	$94,765,165	$103,800,146
Field Inspection and Investigation Costs (ORA)	$22,590,258	$23,260,052
Agency General and Administrative Costs (OC)	$31,081,277	$33,793,942
Total Process Costs	**$480,952,183**	**$524,303,323**
Amount from Appropriations	$211,518,383	$218,659,186
Amount from Fees	$269,433,800	$305,644,137

The costs for all components rose in FY 2006. The increased expenditures primarily reflect mandatory pay increases for all federal employees, increased employee benefit costs, the costs of moving many of the CDER review staff to the new White Oak facility, and an increase in total staff for the review process—from a total of 2,545 Full-time employee equivalents (FTEs) in FY 2005, to a total of 2,691 FTEs in FY 2006.

The Agency General and Administrative Costs have declined steadily over the last 5 years as a percent of total spending on the drug review process. About 7.2 percent of drug review process costs were devoted to agency general and administrative costs in FY 2004, and that declined to 6.5 percent in FY 2005 and 6.4 percent in FY 2006.

MANAGEMENT CHALLENGES FOR FY 2007

Since 1990, FDA has cut in half the time it takes to evaluate new drugs, while still maintaining its traditional rigorous standards for drug safety and effectiveness. This improvement, coupled with other attractive features of the U.S. market, has led to an increase in the number of new drugs launched first in the United States before they are available in other countries, making most new therapies available first to Americans. This is a dramatic shift from the previous 20 years, in which most new drugs were available in the United States years after they were available in other countries. Without the funds derived from PDUFA fees, the substantial progress FDA has achieved in improving and expediting the review of human drug applications would not have been possible.

Under PDUFA III, a more stable revenue structure and increased revenue stream provide FDA with the resources needed to meet PDUFA III performance goals and to embark on several new PDUFA III initiatives aimed at further enhancing the drug review program.

In FY 2007, FDA will continue to build on successes of the PDUFA III IT program by expanding the use of the eCTD format and the FDA ESG. The implementation of the FDA ESG will enable the Centers to standardize the secure e-mail process to provide industry with additional process standardization, as called for in the PDUFA III Electronic Applications and Submission Goals. FDA will also continue to move forward with IT infrastructure consolidation and modernization under the IT Infrastructure Transformation Program. It is critical for FDA to modernize the underlying IT infrastructure so that FDA can continue to make progress in providing a standardized electronic review environment for FDA reviewers.

FDA will continue to be challenged by the need to hire, train, and retain qualified reviewers in FY 2007. A large number of FDA's experienced reviewers are nearing or entering retirement eligibility and their historical knowledge and expertise needs to be retained and passed on. In addition, their skills are in demand and many have excellent employment opportunities available to them. FDA's ability to attract and retain the best and the brightest in medicine and science is critical to maintaining the agency's recognized gold standard in new product safety. In January 2007, in response to the IOM report, "The Future of Drug Safety: Promoting and Protecting the Health of the Public," FDA reaffirmed its commitment to drug safety. FDA's response outlined a comprehensive approach to strengthening the drug safety system, including enhancing the science of drug safety throughout the product life cycle, improving communication among all stakeholders engaged in promoting the safe use of drugs, and improving agency operations and management. Continued PDUFA funding is essential to assure the full implementation of these urgent public health initiatives.

In FY 2007, FDA will complete its work with stakeholders on the development of the terms of draft legislation to reauthorize PDUFA for another 5 years after PDUFA III sunsets at the end of FY 2007. FDA held a public meeting in February 2007, to discuss proposals developed for reauthorization of PDUFA for another 5 years. FDA submitted its proposals to Congress in March 2007, and is ready to discuss these proposals with Congress. Early enactment of PDUFA reauthorization, by early to mid-summer 2007, is crucial to assure stable continuity of operations at FDA and to prevent unwanted staff attrition if employees

become concerned about their job security, which is so dependent on the continuation of PDUFA funding.

Appendix A

CONDITIONS FOR ASSESSMENT AND USE OF FEES

The Federal Food, Drug, and Cosmetic Act (the Act) specifies three major conditions that must be met each year before prescription drug user fees may be collected and spent. A summary of these conditions and how FDA met them appears on page 2. A more detailed description of each of these conditions is provided below, with an explanation of how FDA met the condition in FY 2006.

For making the calculations to determine if statutory conditions are met, an adjustment factor must be used. It is defined in section 735(8) of the Act, as follows:

> The term 'adjustment factor' applicable to a fiscal year is the Consumer Price Index for all urban consumers (all items; United States city average) for April of the preceding fiscal year divided by such Index for April 1997.

The consumer price index for April 2005, the fiscal year preceding FY 2006, was 194.6. The consumer price index for April 1997 was 160.2. The result of this dividing 194.6 by 160.2 is an adjustment factor of 1.2147 for FY 2006.

The **first condition** is based on section 736(f)(1) of the Act. It states:

> Fees under subsection (a) shall be refunded for a fiscal year beginning after FY 1997 unless appropriations for salaries and expenses of the Food and Drug Administration for such fiscal year (excluding the amount of fees appropriated for such fiscal year) are equal to or greater than the amount of appropriations for the salaries and expenses of the Food and Drug Administration for fiscal year 1997 (excluding the amount of fees appropriated for such fiscal year) multiplied by the adjustment factor applicable to the fiscal year involved.

This provision does not allow FDA to collect or spend user fees unless FDA's total Salaries and Expenses appropriation (excluding user fees) each year are greater than or equal to FDA's FY 1997 Salaries and Expenses appropriation (excluding user fees) multiplied by the adjustment factor. FDA's total FY 1997 Salaries and Expenses appropriation (excluding user fees) was $819,971,000. Multiplying this amount by the adjustment factor of 1.2147, an adjusted FY 1997 Salaries and Expenses Appropriation (excluding user fees, and rounded to the nearest thousand dollars) is $996,019,000.

In FY 2006, FDA's total Salaries and Expenses appropriation (excluding user fees and excluding rent to GSA, which was also not included in the FY 1997 appropriation amount) was $1,370,398,000. Because the FY 2006 appropriation exceeded the FY 1997 adjusted amount, the first condition was met.

The **second condition** is stated in Section 736(g)(2)(A)(i): that fees "shall be retained in each fiscal year in an amount not to exceed the amount specified in appropriation acts, or otherwise made available for obligation, for such fiscal year…."

The President signed the Appropriation Act that specified the amounts collectable from prescription drug user fees in FY 2006 ($305,332,000) on November 10, 2005 (Public Law 109-97). Therefore, the second condition was met.

The **third condition** in Section 736(g)(2)(A)(ii), states that fees:

> Shall only be collected and available to defray increases in the costs of the resources allocated for the process for the review of human drug applications (including increases in such costs for an additional number of full-time equivalent positions in the Department of Health and Human Services to be engaged in such process) over such costs, excluding costs paid from fees collected under this section, for fiscal year 1997 multiplied by the adjustment factor.

In FY 1997, FDA's actual obligation for the review process of human drug applications (excluding obligations paid from user fees) was $147,959,689, as reported in the FY 1997 Financial Report to Congress. Multiplying this amount by the adjustment factor of 1.2147, FDA's 1997 adjusted minimum spending for the human drug applications review process from appropriations (exclusive of user fees) was $179,726,634 in FY 2006.

In FY 2006, FDA obligated $218,659,186 from appropriations for the human drug applications review process. Because $218,659,186 is greater than $179,726,634, the third condition was met.

The table below provides the amounts that FDA spent on the review process of human drug applications in FY 2005 and FY 2006, and the adjusted FY 1997 amount that had to be spent from appropriations. It also provides the amounts of these costs derived from appropriations and from user fees in each fiscal year.

FOOD AND DRUG ADMINISTRATION
OBLIGATIONS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2006

	FY 1997 Adjusted for FY 2006	FY 2005	FY 2006
From Appropriations	$179,726,634	$211,518,383	$218,659,186
From User Fee Revenues		$269,433,800	$305,644,137
Total Obligations		$480,952,183	$524,303,323

Appendix B

EXEMPTIONS AND WAIVERS

Beginning in FY 1993, PDUFA directed FDA to waive or reduce fees in five different circumstances:

- when a waiver is necessary to protect the public health;
- when a fee is a significant barrier to innovation;
- when the fees paid exceed FDA's costs of reviewing a firm's human drug applications;
- when imposition of the fee creates an inequity between certain 505(b)(1) and 505(b)(2) human drug applications (This waiver provision was deleted in PDUFA III); and
- when a sponsor withdraws a pending human drug application after FDA has filed it, but before FDA has performed substantial work on the marketing application.

In addition, under PDUFA II, new exemptions from application fees were added beginning in FY 1998. These specific exemptions are automatic and do not require a waiver request. They include:

- human drug applications only for designated orphan products (designated for rare diseases or conditions affecting fewer than 200,000 patients in the United States);
- supplemental applications for pediatric indications for use. (Statutorily repealed by section 5 of Public Law 107-109, effective January 4, 2002).

Beginning in FY 1998, PDUFA II also provided a waiver for certain small businesses for the full application fee for the first application submitted. Before FY 1998, only half of the application fee was waived for small businesses.

The increased number of exemptions required by PDUFA II reduced the number of applications that pay fees.

Fees may be waived or reduced under the waiver provisions of the statute. Many of the application fee waiver requests FDA received through FY 1997 pertained to orphan products; since designated orphan products are now given automatic exemptions, the number of waiver requests for application fees has decreased substantially.

The tables on the following page summarize the exemption and waiver actions taken by FDA for fees payable in the five most recent fiscal years.

EXEMPTIONS AND WAIVERS AS OF SEPTEMBER 30, 2006

Does not Include Data on FY 2007 Waivers Granted in FY 2006

Exempted Application Fees [1]

	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	
Orphan Product	10.0	13.5	19.5	28.5	23.8	
Pediatric Supplements	4.5					[2]
Previously Submitted	7.5	3.0	8.0	3.5	6.0	[3]
Total Exemptions	22.0	16.5	27.5	32.0	29.8	
TOTAL Value of Exemptions	**$6,893,040**	**$8,801,100**	**$15,771,250**	**$21,504,000**	**$22,830,150**	

Waived Fees

APPLICATIONS [1]

Small Business Waivers	6.0	14.3	16.3	12.0	9.8	[4]
Miscellaneous Waivers	1.0	1.0	1.0	12.0	7.0	[5]
Value of Waivers Approved	$2,193,240	$8,134,350	$9,892,875	$16,128,000	$12,853,950	

PRODUCTS

Waivers Approved	14.0	31.9	50.0	27.0	17.0
Value of Waivers Approved	$302,820	$1,033,560	$1,804,000	$1,126,170	$716,210

ESTABLISHMENTS

Waivers Approved	12.3	17.5	22.0	16.5	11.0
Value of Waivers Approved	$1,716,335	$3,673,250	$4,989,600	$4,322,891	$2,904,000

TOTAL VALUE--All Waivers Granted	**$4,212,395**	**$12,841,160**	**$16,686,475**	**$21,577,061**	**$20,635,384**

[1] Applications counted in full-fee equivalents.

[2] The exemption for pediatric supplements was repealed by P. L. 107-109 effective January 4, 2002.

[3] Prior to FY 2002 these were included in the total for Miscellaneous waivers.

[4] Prior to FY 2002 this category was included in counts of applications for which fees were exempted. Applications for all exemptions may not have been received.

[5] Prior to FY 2002 this category also included counts of applications for which fees were exempted because applications had been submitted previously or which were not included in the definition of applications that paid fees.

Appendix C

ALLOWABLE AND EXCLUDED COSTS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS

PDUFA and the related House of Representatives Reports 102-895 and 107-481 ("House Reports"), defines the process for the review of human drug applications and the costs that may be included in that process. Using these definitions (and further refinements identified below) and the methodologies described in this report, the Agency identified those activities that were applicable to the process for the review of human drug applications.

Over 96 percent of amounts obligated are expended within 2 years. Therefore, obligations represent an accurate measure of costs.

User Fee Related Costs

Section 735(6) of the Act defines in general terms the activities necessary for the review of human drug applications (the "human drug review process"). In summary, costs related to the following process activities have been attributed to the process for the review of human drug applications:

- All investigational new drug (IND) review activities, including amendments
- All review activities for new drug applications (NDAs), biologic license applications (BLAs), including supplements and amendments
- Regulation and policy development activities related to the review of human drug applications
- Development of product standards for products subject to review and evaluation
- Meetings between the Agency and the sponsor of a covered application or supplement
- Review of labeling prior to approval of a covered application or supplement and the review of the initial pre-launch advertising
- Review of post-marketing studies that have been agreed to by sponsors as a condition for approval
- Inspections of facilities undertaken as part of the review of pending applications or supplements
- Lot release activities for covered biological products
- Assay development and validation to ensure batch-to-batch consistency and reliability for covered biological products
- Monitoring of clinical and other research conducted in connection with the review of human drug applications
- User Fee Act implementation activities

- Research related to the human drug review process—although under PDUFA II FDA phased out research supported by fee revenues, and
- In the case of drugs approved after October 1, 2002, under human drug applications or supplements: collecting, developing, and reviewing safety information on the drugs, including adverse event reports, during a period of time after approval of such applications or supplements, not to exceed three years—added under PDUFA III.

All user-fee related costs represented by the above activities are collectively referred to in this report as costs for the process for the review of human drug applications.

Section 735(7) of the Act defines the "costs of resources allocated for the process for the review of human drug applications" as the expenses incurred in connection with this process for:

(A) officers and employees of the FDA, contractors of the FDA, advisory committees, and costs related to such officers, employees, committees and contracts;
(B) management of information, and the acquisition, maintenance, and repair of computer resources;
(C) leasing, maintenance, renovation, and repair of facilities and acquisition, maintenance, and repair of fixtures, furniture, scientific equipment, and other necessary materials and supplies; and
(D) collecting user fees under section 736 of the Act and accounting for resources allocated for the review of human drug applications and supplements.

User Fee Excluded Costs

The Act excludes costs related to the following:

Excluded Products

- Generic drugs
- Over-the-counter drugs not associated with an NDA or NDA supplement
- Large volume parenteral drug products approved before September 1, 1992
- Allergenic extract products
- Whole blood or a blood component for transfusion
- In vitro diagnostic biologic products
- Certain drugs derived from bovine blood

Excluded Process Activities

- Enforcement policy development
- Post-approval compliance activities
- Advertising review activities once marketing of the product has begun
- Inspections unrelated to the review of covered applications

- Research unrelated to the human drug review process

These inclusions and exclusions required accounting for a newly created subset of FDA activities after the fact. It was necessary to develop and implement a methodology that would allow the Agency retrospectively to capture the FY 1992 costs for the newly defined "process for the review of human drug applications," and apply that same methodology for future years. In 1995, Arthur Andersen & Company independently reviewed FDA procedures for doing this and found the methodologies reasonable.

Appendix D

DEVELOPMENT OF COSTS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS

GENERAL METHODOLOGY

The costs associated with the process for the review of human drug applications are based on obligations recorded within FDA's Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), Office of Regulatory Affairs (ORA), and the Office of the Commissioner (OC). These organizations correspond to the cost categories presented on the Statement of Costs for the Process for the Review of Human Drug Applications as follows:

Cost Category	FDA Organization
Costs for the Review of New Drug Applications (NDA's), Biologic License Applications (BLA's), and Supplements	CDER
Costs for the Review of BLA's and Supplements	CBER
Field Inspection and Investigation Costs	ORA
Agency General and Administrative Costs	OC

The costs were accumulated using time reporting systems in CDER, CBER, and ORA, and were extrapolated for OC. Using the definitions of costs and activities included in the "process for the review of human drug applications" in the Act, a portion of the costs within each of the four organizations listed above was identified as part of the human drug review process.

CENTER COSTS

Costs are accumulated in CDER and CBER in cost centers corresponding to the organizational components (usually divisions) within the Centers. Most FDA components involved in the human drug review process perform a mixture of activities--some included in the definition of the process for the review of human drug applications, and some not included. These components fall into three categories: 1) direct review and laboratory components; 2) indirect review and support components; and 3) center-wide expenses. The allocation of costs for the three categories is discussed below.

Direct Review and Laboratory Components

Employees in all components of CDER and CBER, other than those noted below as center indirect review and support components, reported their time for eight weeks during FY 2006 in activities that could be used to differentiate between time spent on the process for the review of human drug applications and all other time.

Both CDER and CBER time reporting systems were modified after the enactment of PDUFA, so that time could be reported in activities that could be separated into allowable and excluded activities with respect to the process for the review of human drug applications, as defined in PDUFA and as further explained in Appendix C. This method for determining allowable and excluded costs for PDUFA direct review and laboratory costs has been used consistently, with only minor modifications, since 1993, when costs were initially measured by Arthur Andersen & Company. Beginning in FY 1996, the CBER time reporting system was enhanced to collect on-line time reports for all employees other than management and administrative support personnel for a 2-week period each quarter of the fiscal year. The enhanced system reports time for 50 possible functional activities, by 7 product classes.

In November 1997, CDER initiated an on-line time reporting survey of each employee within the Center. Beginning in FY 2001, this survey captures the expenditure of time on activities that are part of the process for the review of human drug applications and all other CDER mission-oriented activities for two 4-week periods—one in each half of the fiscal year.

A similar procedure is used in CBER's direct review and laboratory components to measure costs for the process for the review of human drug applications. CBER's time reporting system was validated by studies just after PDUFA was initiated. That system collects time reports on-line from all employees other than management and administrative support personnel for a 2-week period during each quarter of the fiscal year.

FDA Centers are very payroll-intensive organizations – 61 percent of all FDA funds pay for employee salaries and benefits, and almost all other costs are directly supporting these employees. Thus the average percentage of time reported each year during this 8-week period (2 weeks each quarter for CBER, and 4 weeks semiannually for CDER) as having been expended on drug review process activities for each cost center is then applied to all costs incurred for each cost center for the entire fiscal year to estimate the costs for each cost center that were part of the process for the review of human drug applications.

Center Indirect Review and Support Components

Indirect review and support components provide the infrastructure for the review process. In CDER, these components include portions of the Office of the Center Director, the Office of Regulatory Policy, the Office of Business Process Support, the Office of Management, the Office of Training and Communications, the Office of Medical Policy, the Office of Executive Programs, and the Office of Compliance. In CBER, these components include portions of the Office of the Center Director, Office of Management, Office of Information

Management, and the Office of Communications, Training, and Manufacturers Assistance. Most employees of these components do not report their time.

Instead, the time of the management and administrative support personnel is assumed to be the average percentage time of all Center employees in direct review and laboratory components who reported their time. Thus the average percentage of time reported each year during this 8-week period as having been expended on drug review process activities for all direct review and laboratory components was then applied to all costs incurred for the entire fiscal year by the indirect review and support components.

Center-Wide Expenses

A number of Center-wide expenses are paid from central FDA accounts rather than charged directly to a specific Center. These costs include rent for facilities that house drug review staff, telecommunications and utility costs, some computer equipment and support costs, facilities repair and maintenance, and some extramural and service contracts. Many of these costs were traced back to the specific division that generated the cost and were assigned the user fee percentage calculated for the division to which the expenditure related. For the costs that benefited the Center as a whole and could not be traced to a specific division, a weighted average user fee percentage was calculated based on the level of user fee related costs to total costs in the Center.

In support of the President's Management Agenda and Secretarial Goal of "One-HHS," FDA consolidated administrative functions from the Centers and the Office of Management (including facilities, procurement, finance, EEO, and IT services) into the Office of Shared Services in FY 2004. The goal of implementing the Office of Shared Services is to keep the administrative functions related to the review costs more efficient.

In the FY 2006 financial report, the resources that were previously provided by the Centers, but are now provided by the Office of Shared Services, are reported as if they were still performed by the Centers, in order to make the FY 2006 report comparable with the reports of previous years.

CENTER RESEARCH COVERED BY THE PRESCRIPTION DRUG USER FEE ACT

Research activities supporting the process for the review of human drug applications were included when FDA originally calculated base costs for the process for the review of human drug applications for FY 1992 and FY 1993. Under PDUFA I, from FY 1993 through FY 1997, both appropriated funds and user fee revenues were used to fund research activities supporting the drug review process, just as was the case with all other PDUFA activities. During informal discussions that led to PDUFA II, FDA agreed to phase out the use of fee revenues to support these research costs. The phase-out was complete in FY 2001. The remaining research related to the drug review process is now supported solely by appropriated funds, just as it was prior to FY 1993.

CENTER TIME REPORTING RESULTS FOR FY 2006

The time reporting systems operated by CBER and CDER indicated the 65 percent of all time spent in CBER and 78 percent of all time spent in CDER in FY 2006 was dedicated to the process for the review of human drug applications as defined in PDUFA.

FIELD INSPECTION AND INVESTIGATION COSTS

FDA's ORA incurs all field inspection and investigation costs. ORA costs are incurred in both district offices (the "field") and headquarters support offices. In FY 2002, the agency began tracking accumulated ORA costs through the use of the Field Accomplishment and Compliance Tracking System [FACTS]. FACTS is a time and activity tracking system which captures time in a variety of categories, including pre-approval inspections of manufacturing facilities, investigations of clinical studies, and analytical testing of samples--which are included in the process for the review of human drug applications.

Total direct hours reported in FACTS are used to calculate the total number of staff-years required by ORA to perform these activities. In addition to the direct time, an allocation of support time is also included to represent the work done by the ORA administrative and management personnel. The agency then applies the total number of user fee related staff years to the average salary cost in ORA to arrive at ORA user fee related salary costs. The final step is to allocate ORA obligations for operations and rent to the human drug review process based upon the ratio of user fee related staff years to total ORA staff years. The following table summarizes the calculation of ORA costs for the review of human drug applications for FY 2005 and FY 2006.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2006

Cost Component	FY 2005	FY 2006
Staff Years Utilized	145	142
ORA Average Salary and Benefits	$93,594	$99,675
Salary and Benefits	$13,571,103	$14,153,875
Operations, Rent, and Shared Services	$9,019,155	$9,106,177
TOTAL	**$22,590,258**	**$23,260,052**

The ORA costs for the process for the review of human drug applications described above include total process costs, including costs paid from appropriations and costs paid from fee revenues.

AGENCY GENERAL AND ADMINISTRATIVE COSTS

The agency general and administrative costs are incurred in the FDA's OC. During most of FY 2006, OC was comprised of the following offices:

- Immediate Office of the Commissioner
- Office of the Chief Counsel
- Office of Equal Employment Opportunity and Diversity Management
- Office of the Administrative Law Judge
- Office of Science and Health Coordination
- Office of International Activities and Strategic Initiatives
- Office of Crisis Management
- Office of Legislation
- Office of External Relations
- Office of Policy and Planning
- Office of Management

The OC costs applicable to the process for the review of human drug applications were calculated using a method prescribed by the Division of Cost Determination Management, Office of Finance, Office of the Assistant Secretary for Resources and Technology, Office of the Secretary, Department of Health and Human Services. The method uses the percentage derived by dividing total OC costs by the total salary obligations of the agency, excluding the OC. That percentage is then multiplied by the total salaries (excluding benefits) applicable to the process for the review of human drug applications in CDER, CBER, and ORA to arrive at the total General and Administrative Costs.

Using this process, $31,081,277 and $33,793,968 in general and administrative obligations were dedicated to the human drug review process in FY 2005 and FY 2006, respectively. They are the total costs, including the funds obligated both from appropriations and user fees. The agency general and administrative obligations in FY 2006 accounted for 6.4 percent of the total costs of the human drug application review process. This is down from FY 2005, when general administrative obligations accounted for 6.5 percent of the costs of the human drug applications review process. This continues a downward trend over the last several years. This percentage has steadily declined from the 10.4 percent reported in the FY 1998 PDUFA Financial Report.

Appendix E

RISK MANAGEMENT COMPONENT OF COSTS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS

REQUIREMENT FOR THIS APPENDIX

PDUFA III expanded the definition of the drug review process to include collecting, developing or reviewing safety information on drugs, including adverse event reports, for up to 3 years after a product is approved. The performance goals letter specifies that FDA is to allocate $70.9 million in user fees over 5 years to these activities and that FDA will include in its annual report to Congress an accounting of this spending. This appendix responds to this requirement.

INITIAL PLAN FOR RISK MANAGEMENT SPENDING

In July 2003 FDA published its PDUFA III Five-Year Plan that included information on its plan to spend the risk management funds. The table below provides a summary of those plans.

Summary Risk Management Spending Plan
From FDA's July 2003 PDUFA III Five-Year Plan
($000)

	FY 2003 Plan	*FY 2004 Plan*	*FY 2005 Plan*	*FY 2006 Plan*	*FY 2007 Plan*
Additional Staff Years	*19*	*34*	*56*	*84*	*96*
Payroll for Additional Staff Years	*$2,020*	*$3,721*	*$6,539*	*$10,160*	*$12,218*
Operating Support	*$231*	*$420*	*$730*	*$1,129*	*$1,359*
Contract Support	*$4,480*	*$5,172*	*$6,273*	*$4,608*	*$5,079*
GSA Rent & Rent Related	*$183*	*$328*	*$551*	*$835*	*$998*
Central Support	*$240*	*$429*	*$734*	*$1,132*	*$1,375*
TOTAL	***$7,154***	***$10,070***	***$14,827***	***$17,864***	***$21,029***

ACTUAL RISK MANAGEMENT OBLIGATIONS

The table below shows amounts FDA has obligated for risk management activities as of the end of FY 2003 to FY 2006, and the planned obligations for FY 2007 that remains unchanged from the original plan.

Risk Management Funds Obligated as of September 30, 2006
and planned for obligation in FY 2007
($000)

	FY 2003 Actual	FY 2004 Actual	FY 2005 Actual	FY 2006 Actual	*FY 2007 Plan*
Additional Staff Years	19	37	62	100	*96*
Payroll for Additional Staff Years	$2,270	$4,695	$7,401	$12,339	*$12,218*
Operating Support	$204	$292	$463	$1,005	*$1,359*
Contract Support	$3,974	$5,349	$6,193	$6,686	*$5,079*
GSA Rent & Rent Related	$181	$204	$551	$1,437	*$998*
Central Support	$244	$615	$806	$1,514	*$1,375*
TOTAL	**$6,873**	**$11,155**	**$15,414**	**$22,981**	**$21,029**

As the table above shows, FDA has spent slightly less than planned in FY 2003 and slightly more than planned in FY 2004 to FY 2006. At this rate, FDA expects to spend at least the expected $70.9 million on risk management activities over the course of PDUFA III.

The FTE for risk management funded over the period FY 2003 to FY 2006, and planned for FY 2007, broken out by Center, are provided in the following table.

FTE PAID FROM RISK MANAGEMENT FUNDS as of September 30, 2006
and planned for obligation in FY 2007

Component	FY 2003 Actual	FY 2004 Actual	FY 2005 Actual	FY 2006 Actual	*FY 2007 Plan*
CDER	11	26	51	86	*78*
CBER	5	7	7	9	*12*
OC	3	4	4	5	*6*
FDA Total	**19**	**37**	**62**	**100**	**96**

Additional funding for risk management activities from PDUFA fees has enabled FDA to increase its public health and consumer protection efforts in overseeing the safety of newly approved drug products during their first two or three years on the market. PDUFA risk management funds have made it possible to increase the number of staff responsible for assuring the safety of drug products during the periapproval period. FDA has been able to hire more scientists, including epidemiologists, drug utilization specialists, and safety evaluators.

Fees have also been used to partially finance operations expenses for the primary safety evaluator tool, the Adverse Event Reporting System. In the last few years, FDA has experienced a substantial increase in reports of drug adverse events. Additional resources have helped ensure that adverse event reports are entered in an accurate, complete, and timely manner.

Fees have also enabled FDA to continue to fund drug utilization contracts to supply the agency with data on drug use. These data provide important information regarding numbers of dispensed prescriptions, patient demographics, diagnoses, trends over time, and sales volume for various groups such as outpatients, inpatients, and children. User fees have provided resources to make these databases available for investigation of important safety signals identified during surveillance.