FY 2007 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

JULY 2008

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

AUG 15 2008

The 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 2007 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 enables FDA to strengthen its drug review process and meet the performance goals established for this program.

I appreciate the timely action of Congress in reauthorizing PDUFA for an additional 5 years in the Food and Drug Administration Amendments Act of 2007.

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) 2007.

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 2007. The statements and tables included in this report also provide the user fee revenues and expenditures in FY 2007, the carryover balance, and comparative data for earlier periods.

For FY 2007, FDA collected $376 million in fees, including fees collected for earlier periods. This is more than the $352 million FDA projected at the beginning of the year when fees for FY 2007 were established. The higher revenue is attributable to receiving a greater than anticipated number of fee-paying applications.

In FY 2007, FDA obligated $320 million from PDUFA fee revenues. This accounted for about 56 percent of all funds obligated by FDA from all sources in support of the process for the review of human drug applications. This $320 million was about $56 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 $131 million at the end of FY 2007. 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 2008 include hiring and training of additional staff and maintaining existing staff to assure that FDA meets the PDUFA IV goals and maintains application review productivity.

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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 (PDUFA II) and 2002 (PDUFA III). FY 2007 was the last year of PDUFA III, although the program was reauthorized for another 5 years (PDUFA IV) in 2007.

Under PDUFA, 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 2007 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 2007 PDUFA Financial Report, covering the period from October 1, 2006, to September 30, 2007.

As required by the statute, this report presents 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 2007. This report also presents summary statements of FY 2007, 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.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 2007

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 2007 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 2007, 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 $1,442,373,000. 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 $1,031,360,000. Therefore, since the FY 2007'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 110-5) specifying amounts collectable from fees during FY 2007, on February 15, 2007. It provided for $352,200,000 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 $186,103,687. In FY 2007, FDA obligated $254,576,372 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 PDUFA USER FEE REVENUES BY FEE SOURCE
As of September 30, 2007

Fiscal Year	FY 2006	FY 2007
Fees Collected:		
Application Fees	$102,661,542	$126,414,551
Establishment Fees	$110,518,981	$125,368,514
Product Fees	$101,363,865	$108,405,265
TOTAL FEES COLLECTED:	**$314,544,388**	**$360,188,330**
Fee Receivables:		
Application Fees	$0	$448,100
Establishment Fees	$396,000	$782,750
Product Fees	$379,170	$398,000
TOTAL FEES RECEIVABLE:	**$775,170**	**$1,628,850**
Total User Fee Revenues:	**$315,319,558**	**$361,817,180**

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 2006, even if it is received in FY 2007, is attributed to FY 2006 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. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C. In FY 2007, FDA obligated $320,429,620 from user fee revenues.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF PDUFA FEE OBLIGATIONS BY EXPENSE CATEGORY
As of September 30, 2006 and 2007

Expense Category	FY 2006	FY 2007
Personnel Compensation and Benefits	$188,550,842	$200,031,909
Travel and Transportation	$3,109,474	$4,304,157
Rent	$14,100,000	$9,001,000
Communications	$4,377,218	$5,218,200
Contract Services	$87,831,998	$86,710,548
Equipment and Supplies	$6,782,580	$11,956,385
Other	$892,025	$3,207,421
TOTAL OBLIGATIONS:	**$305,644,137**	**$320,429,620**

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. More detailed information about the development of the costs associated with the review of human drug applications can be found in Appendix D.

In FY 2007, PDUFA fees and appropriations paid for 1,461 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 2007 totaled about 60 percent of the obligations. This includes all pay and benefits for the additional personnel.

During FY 2007, both CBER and CDER fully automated the electronic submission process by implementing automated systems to expedite the processing and increase the availability of properly formatted FDA Electronic Submissions Gateway (ESG) submissions. The ESG received and processed over 147,000 pre-market and post-market submissions. Most of these submissions were post-marketing safety reports. During the last 6 months of FY 2007, the ESG was processing over 13,800 post-market safety reports per month. In the pre-market area, the ESG was averaging over 1100 submissions per month. Information on the ESG process and requirements are available at: http://www.fda.gov/esg/. The electronic submission process encompasses the receipt, acknowledgment of receipt, and any processing errors (to the sender), routing, notification (to a receiving Center or Office), and providing access to the review team of the electronic submission. The implementation of the ESG

enabled CBER and CDER to establish a common process in the exchange of secure e-mail. The FDA eCTD (Electronic Common Technical Document) review system was enhanced to provide integration with the CBER and CDER tracking systems. In FY 2007, there was a dramatic increase in the number of eCTD submissions with over 8,000 eCTD submissions received. Since FY2003, CBER and CDER have received over 14,000 eCTD submissions. The eCTD guidance and specifications are available at: http://www.fda.gov/cder/regulatory/ersr/ectd.htm. These major initiatives enabled 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.

CDER and CBER also collaborated on an information management system development effort to integrate electronic workflow and tracking information to process and manage regulatory submissions. The initial release handled therapeutic IND submissions. In early FY2008, the system will be expanded to include all CDER INDs. Future releases will incorporate CDER and CBER marketing applications and CBER INDs. In addition, 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 FY2007, the FDA successfully completed implementation of HHS Enterprise E-mail System (EES). The EES consolidated the various email systems throughout HHS into a single enterprise e-mail and calendaring system.

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 2007 increased the carryover balances by $55,167,653. Much of this increase was the result of the final year adjustment to PDUFA fees made to assure that FDA would have at least 3 months of operating reserves at the end of FY 2007, when the PDUFA III authorization law expired.

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	Fee Revenue 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	$283,491,495	$269,433,800	$65,789,792
2006	$65,789,792	$315,502,786	$305,644,137	$75,648,440
2007	$75,648,440	$375,597,273	$320,429,620	$130,816,093
2008	$130,816,093			

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 2007 of $375,597,273 is greater than the FY 2007 collections balance on page three ($360,188,330). This is because the FY 2007 net collections figure also includes some prior years' receivables that FDA collected in FY 2007. 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 first such offset (for excess collections in 1998 and 2004) was made when fees were set for FY 2007, as reflected in the table below. At the time fees were set for 2007 (August 2006), there were no excess collections for other years. Collections since then have resulted in additional excess collections. 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. Under the provisions of PDUFA IV, the next offset for additional excess collections will be made when fees are set for FY 2012.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF FEES COLLECTED, COLLECTION CEILINGS, AND POTENTIAL REFUNDS
As of September 30, 2007

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	$87,756,811	$87,528,000	$228,811	
1998	$117,849,016	$117,122,000		$727,016
1999	$125,729,367	$132,273,000		-
2000	$141,134,682	$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	$258,316,700	$249,825,000		$8,491,700
2005	$287,178,231	$284,394,000		$2,784,231
2006	$314,544,388	$305,332,000		$9,212,388
2007	$360,188,388	$305,332,000		$7,988,330
		Total:	**$232,576**	**$29,203,665**
Amount Offset When Fees for FY 2007 Were Determined				$7,957,922
Balance Remaining to be Offset When fees are set for 2012				**$21,245,743**

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 ($228,811), 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. In addition, a number of other requests for refunds or waivers are pending. Until refund and waiver requests are settled, however, FDA will keep $2,500,000 in reserve as an offset for future refunds.

FY 1998 collections exceeded the appropriations limit by $727,016. In FY 2004, collections exceeded the appropriation limit by $8,491,700; in FY 2005 collections exceeded the appropriation limit by $2,784,231; in FY 2006 collections exceeded appropriations by a total of $9,212,388; and in FY 2007 collections exceeded appropriations by a total of $7,988,330. Since 1998, collections have exceeded appropriations by a total of $29,203,665. 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 $21,245,743 remains to be offset. Under PDUFA IV, an offset will be made when fees are set in 2012 for the cumulative amount of excess collections, through FY 2010 and projected through 2011. In the meantime, this $21,245,743 must be held in reserve for an offset in FY 2012, unless collections in the years from 2008 through 2011 should fall below amounts appropriated for user fees in those years. The amount to be held in reserve for future offset will be recalculated in the annual financial report each year.

OTHER RESERVES AND BALANCE AVAILABLE FOR ALLOCATION

The table below provides a summary of carryover balances as of September 30, 2007, and anticipated claims on those balances.

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 2012. The carryover amount shown as available for allocation in the table below ($107,070,350) is enough to fund estimated FY 2008 operations for approximately 2.8 months.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CARRYOVER BALANCE
As of September 30, 2007

Status of Carryover Funds	Amount
Reserve for Refunds	$2,500,000
Reserve for Future Collection Offset	$21,245,743
Available for Allocation	$107,070,350
TOTAL Carryover Balance	$130,816,093

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 2006 and FY 2007 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, 2007

FDA Component	FY 2006	FY 2007
Center for Drug Evaluation and Research (CDER)	$363,449,183	$385,939,977
Center for Biologics Evaluation and Research (CBER)	$103,800,146	$122,871,873
Field Inspection and Investigation Costs (ORA)	$23,260,052	$25,860,072
Agency General and Administrative Costs (OC)	$33,793,942	$40,334,070
Total Process Costs	**$524,303,323**	**$575,005,992**
Amount from Appropriations	$218,659,186	$254,576,372
Amount from Fees	$305,644,137	$320,429,620

Of the total of $575,005,992 obligated in support of the process for the review of human drug applications as defined in PDUFA, about 56 percent came from PDUFA fees and about 44 percent came from appropriations. The costs for all components increased in FY 2007. The increases in expenditures primarily reflect mandatory pay increases for all Federal employees and increased employee benefit costs. In FY 2007, a total of 2,738 FTEs were expended in support of the process for the review of human drug applications as defined in PDUFA.

MANAGEMENT CHALLENGES FOR FY 2008

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.

2008 will be the first year of PDUFA IV. FDA will have a more stable revenue structure and increased revenue stream to provide FDA with the resources needed to meet PDUFA IV performance goals and to embark on several new PDUFA IV initiatives aimed at further enhancing the drug review program.

In FY 2008, FDA will focus on developing the PDUFA IV IT Plan that will be published for public comment before finalizing the PDUFA IV IT Plan by May 30, 2008. With the expansion of the PDUFA program into the post-market area, FDA will focus efforts on improving the post-market IT systems. The improvement of the drug safety IT systems is part of an agency project to consolidate the reporting of product safety information. FDA will continue to move forward with the development of a common PDUFA information management system to integrate electronic workflow and tracking information to process and manage regulatory submissions.

FDA will also continue to move forward with IT infrastructure consolidation and modernization. It is critical for FDA to modernize the underlying IT infrastructure so that it can continue to make progress in providing a standardized electronic review environment for its reviewers. The construction of the White Oak Data Center will replace existing computer facilities that maintain database, application, web, storage and network servers, minicomputers and telecommunication equipment. The data center consolidation will facilitate server consolidation efforts, which will allow FDA to realize savings on hardware and software licensing, hardware and software maintenance, systems support and training, and on hardware through purchase consolidation. The data center is scheduled to be completed in the latter part of 2008.

In FY 2008, FDA will continue to be challenged by the need to hire and train additional reviewers and support staff as well as by the need to retain qualified reviewers. 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 FY 2008, FDA will also be challenged with implementing the many important new provisions of the FDA Amendments Act (FDAAA) of 2007. Signed into law on September 27, 2007, FDAAA provides the agency with new authorities to ensure drug safety and new responsibilities to disseminate more timely and comprehensive drug information to the public. The new law adds user fee funding to support these important new activities. FDA must develop the procedures, guidance, and information infrastructure, and engage both public and private stakeholders in new partnerships, to perform this work in the most effective way to ensure both the availability and safe use of new drug products. Continued PDUFA funding is essential to assure the effective implementation of these important provisions and related public health initiatives.

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 two. A more detailed description of each of these conditions is provided below, with an explanation of how FDA met the condition in FY 2007.

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 2006, the fiscal year preceding FY 2007, was 201.5. The consumer price index for April 1997 was 160.2. The result of dividing 201.5 by 160.2 is an adjustment factor of 1.2578 for FY 2007.

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 1.2578, an adjusted FY 1997 Salaries and Expenses Appropriation (excluding user fees, and rounded to the nearest thousand dollars) is $1,031,360,000.

In FY 2007, 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, 442,373,000. Because the FY 2007 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 from prescription drug user fees in FY 2007 ($352,200,000) on February 15, 2007 (Public Law 110-5). 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 1.2578, FDA's 1997 adjusted minimum spending for the human drug applications review process from appropriations (exclusive of user fees) was $186,103,697 in FY 2007.

In FY 2007, FDA obligated $254,576,372 from appropriations for the human drug applications review process. Because $254,576,372 is greater than $186,103,697, the third condition was met.

The table below provides the amounts that FDA spent on the review process of human drug applications in FY 2006 and FY 2007, 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, 2007

	FY 1997 Adjusted for FY 2007	FY 2006	FY 2007
From Appropriations	$186,103,697	$218,659,186	$254,576,372
From User Fee Revenues		$305,644,137	$320,429,620
Total Obligations		$524,303,323	$575,005,992

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, 2007

Does not Include Data on FY 2008 Waivers Granted in FY 2007

Exempted Application Fees [1]

	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007
Orphan Product	13.5	19.5	28.5	23.8	21.3
Previously Submitted	3.0	8.0	3.5	6.0	4.5
Total Exemptions	16.5	27.5	32.0	29.8	25.8
TOTAL Value of Exemptions	**$8,801,100**	**$15,771,250**	**$21,504,000**	**$22,830,150**	**$23,077,150**

Waived Fees

APPLICATIONS [2]

Small Business Waivers	14.3	16.3	12.0	11.0	10.0
Miscellaneous Waivers (Includes PEPFAR)	1.0	1.0	12.0	12.0	14.0
Value of Waivers Approved	$8,134,350	$9,892,875	$16,128,000	$17,650,200	$21,508,800

PRODUCTS

Waivers Approved	31.9	50.0	27.0	16.0	12.0
Value of Waivers Approved	$1,033,560	$1,804,000	$1,126,170	$674,080	$597,000

ESTABLISHMENTS

Waivers Approved	17.5	22.0	16.5	11.7	7.0
Value of Waivers Approved	$3,673,250	$4,989,600	$4,322,891	$3,091,704	$2,202,972

TOTAL VALUE--All Waivers Granted	**$12,841,160**	**$16,686,475**	**$21,577,061**	**$21,415,984**	**$24,308,772**

[1] Actual number of Exempted Applications received in FY 2007, in full fee equivalents.

[2] Actual Number of Application Fee Waivers Granted in FY 2007--number of waived applications actually submitted may have been smaller.

Appendix C

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

Over 96 percent of amounts FDA obligates (contractually promises to pay) each year are expended within 2 years. Therefore, obligations represent an accurate measure of costs and are the basis of the costs reported in this document.

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, the further refinements described below, and the methodologies described in this report, FDA identified those activities that were applicable to the process for the review of human drug applications.

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 NDAs, 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 FDA 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 (NDAs), Biologic License Applications (BLA's), and Supplements	CDER
Costs for the Review of BLAs 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 2007 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 which captures the expenditure of time on activities that are part of the process for the review of human drug applications and all CDER mission-oriented activities of each employee within the Center for a 2-week period each quarter of the fiscal year. Beginning in FY 2001, the timing of this survey was changed to 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 payroll-intensive organizations – over 60 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.

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 total 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 2007 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 2007 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 2007

The time reporting systems operated by CBER and CDER indicated that 67 percent of all time spent in CBER and 77 percent of all time spent in CDER in FY 2007 was dedicated to the process for the review of human drug applications as defined in PDUFA.

FIELD INSPECTION AND INVESTIGATION COSTS

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, FDA 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 2006 and FY 2007.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2006 and 2007

Cost Component	FY 2006	FY 2007
Staff Years Utilized	142	144
ORA Average Salary and Benefits	$99,675	$104,700
Salary and Benefits	$14,153,875	$15,076,800
Operations, Rent, and Shared Services	$9,106,177	$10,783,272
TOTAL	**$23,260,052**	**$25,860,072**

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. At the end of FY 2007, OC was comprised of the following offices:

- Immediate Office of the Commissioner
- Office of the Chief Counsel
- Office of the Chief of Staff
- Office of the Administrative Law Judge
- Office of Equal Employment and Diversity Management
- Office of International and Special Programs
- Office of Operations
- Office of Policy, Planning and Preparedness
- Office of Scientific and Medical Programs

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, HHS. 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, $33,793,968 and $40,334,070 in general and administrative obligations were dedicated to the human drug review process in FY 2006 and FY 2007, respectively. They are the total costs, including the funds obligated both from appropriations and user fees. The agency general and administrative obligations in FY 2007 accounted for about 7 percent of the total costs of the human drug application review process. This is up slightly from the numbers of the previous two fiscal years (about 6.5 percent in FY 2005 and FY 2006). This percentage has declined significantly 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 over the 5 years of PDUFA III.

Risk Management Funds Obligated as of September 30, 2007
($000)

	FY 2003 Actual	FY 2004 Actual	FY 2005 Actual	FY 2006 Actual	FY 2007 Actual
Additional Staff Years	19	37	62	100	99
Payroll for Additional Staff Years	$2,270	$4,695	$7,401	$12,339	$13,574
Operating Support	$204	$292	$463	$1,005	$493
Contract Support	$3,974	$5,349	$6,193	$6,686	$6,517
GSA Rent & Rent Related	$181	$204	$551	$1,437	$1,224
Central Support	$244	$615	$806	$1,514	$2,249
TOTAL	**$6,873**	**$11,155**	**$15,414**	**$22,981**	**$24,058**

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 2007. FDA spent $80.5 million on risk management activities over the course of PDUFA III —substantially more than the $70.9 million agreed to in the performance goal letter.

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

FTE PAID FROM RISK MANAGEMENT FUNDS as of September 30, 2007

Component	FY 2003 Actual	FY 2004 Actual	FY 2005 Actual	FY 2006 Actual	FY 2007 Actual
CDER	11	26	51	86	78
CBER	5	7	7	9	16
OC	3	4	4	5	5
FDA Total	**19**	**37**	**62**	**100**	**99**

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 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.