FY 2004 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

MARCH 2005

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

May 10, 2005

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

Dear Mr. President:

Enclosed for your consideration is the annual financial report to Congress required by the Prescription Drug User Fee Act of 1992 (PDUFA), as amended. In FY 2002 Congress reauthorized PDUFA for five years (PDUFA III). This is the second financial report under PDUFA III. This report covers fiscal year (FY) 2004 and documents how the Food and Drug Administration (FDA) met each of the conditions specified in PDUFA, thereby allowing the Agency to continue to collect prescription drug user fees.

The report also presents the user fee revenues and related expenses for FY 2004 and comparative data for earlier periods, and details the amounts carried over at the end of each year that remain available. For FY 2004, FDA collected $246 million in user fees and spent $232 million. FDA spent almost 60 percent of the fee revenue for employee salaries and benefits. This infusion of human resources continues to be the single most critical factor enabling FDA to meet the challenging performance goals associated with PDUFA.

Sincerely,

/s/

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 law requires 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 of 1992 (PDUFA), as amended. This report covers fiscal year (FY) 2004.

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 2004. The statements and tables included in this report also provide information on the user fee revenues and expenditures in FY 2004, on the carryover balance, and on comparative data for earlier periods.

For FY 2004, FDA collected $246 million in fees. This is slightly more than the $241 million FDA projected at the beginning of the year when fees for FY 2004 were established. The higher revenues is attributable to receiving a greater than anticipated number of fee paying applications.

In FY 2004, FDA obligated $232 million from PDUFA revenues. This accounted for about 53 percent of all funds obligated in support of the process for the review of human drug applications. FDA obligated about $16 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 $51 million at the end of FY 2004.

Challenges facing FDA in FY 2005 include hiring, training and maintaining the staff to meet the PDUFA III goals and maintaining application review productivity while appropriated budget authority that supports drug review requires FDA to absorb the costs of pay increases and achieve significant administrative efficiencies.

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BACKGROUND

Enacted in 1992, PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. 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 it on 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 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 2004 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 2004 PDUFA Financial Report, covering the period from October 1, 2003 to September 30, 2004.

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 2004. This report also presents summary statements of FY 2004 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.

In keeping with the requirements of the Chief Financial Officers Act of 1990, the Office of the Inspector General (OIG), Department of Health and Human Services, audits FDA's annual financial statements. The audit covers all of FDA's financial systems and funds, including PDUFA revenues and expenses. The OIG issued unqualified audit opinions on FDA's financial statements for fiscal years 1998 through 2004. This is the most favorable category of audit opinion.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 2004

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 2004 are summarized below.

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 2004, FDA's overall Salaries and Expenses Appropriation (excluding user fees and excluding rent to GSA, which was also not included in the FY 1997 Appropriation amount) totaled $1,267,368,000. 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 $940,753,000. Therefore, since the FY 2004'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. For FY 2004, FDA's Appropriation Act, signed by the President on January 23, 2004, specified that $249,825,000 would come from PDUFA fees, in addition to sums provided in regular appropriations. 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 $169,754,151. In FY 2004, FDA obligated $204,775,036 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 on 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 how they are adjusted in each year for inflation and workload. FDA then establishes fees in an effort to assure 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, 2004

	FY 2003	FY 2004
Fees Collected:		
Product Fees	$76,852,785	$76,453,520
Establishment Fees	$78,209,219	$82,318,894
Application Fees	$62,684,550	$87,693,991
TOTAL FEES COLLECTED:	**$217,746,554**	**$246,466,405**
Fees Receivables:		
Product Fees	$194,400	$252,560
Establishment Fees	$314,850	$348,345
Application Fees	-	-
TOTAL FEES RECEIVABLES:	**$509,250**	**$600,905**
Total User Fee Revenues:	**$218,255,804**	**$247,067,310**

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 2003, even if it is received in FY 2004, is attributed to FY 2003 revenues. Totals reported for each year are net of any refunds for that year.

The receivables for FY 2003 and FY 2004 are from uncollected product and establishment fees. 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 2004, FDA obligated $232,081,500 from user fee revenues.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
As of September 30, 2004

Expense Category	FY 2003	FY 2004
Personnel Compensation and Benefits	$130,939,056	$149,446,313
Travel and Transportation	$4,527,825	$4,233,473
Rent	$8,719,000	$6,146,584
Communications	$1,284,635	$2,462,652
Contract Services	$43,500,289	$60,829,302
Equipment and Supplies	$10,246,121	$8,575,391
Other	$937,574	$387,785
TOTAL OBLIGATIONS:	**$200,154,500**	**$232,081,500**

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 2004, PDUFA fees and appropriations paid for 1,284 more staff-years than were used in 1992 for the review process of human drug applications. Employee salary and benefits paid from user fees in FY 2004 totaled over 60 percent of the obligations. This includes all pay and benefits for the additional personnel.

In FY 2004, FDA continued to mature its formal Agency IT investment governance process with direct involvement of the FDA's Management Council and with the establishment of an Agency Enterprise Architecture Review Board (EARB). Specifically, the Agency integrated the PDUFA IT investment governance process with the Agency IT investment process to ensure alignment and linkage to Agency strategic goals. To assist the governance process FDA implemented an Agency IT Portfolio Management System to document and track IT investments starting with the FY 2005 budget cycle. Since the initial implementation, FDA has enhanced the Portfolio Management tool to incorporate Department, Agency, and Center tracking and reporting requirements. The Portfolio Management tool is used throughout the investment process to validate and track the IT investment portfolio in support of the FDA

mission and enterprise architecture target, and to facilitate prioritizing, approving, and monitoring IT investments for the entire Agency.

In March 2004, all Center, ORA and OC IT Directors and their supporting staff started reporting directly to the CIO. Through this framework the CIO is able to work more closely with IT Directors and their customers to ensure their service demands are met, while consistently meeting the demands of FDA, HHS and OMB. It provides a means to drive technology change in a uniform way through direct communication and for ensuring that all IT infrastructure and IT investments support the Agency's common IT goals, fit into a common computing environment and follow good IT management practices.

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 2004 increased the carryover balances by $212,991,344.

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			

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 2004 of $251,617,821 is greater than the FY 2004 collections balance on page 3 ($246,466,405). This is because $251,617,821 contains some prior years' receivables that FDA collected in FY 2004.

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 must 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, 2004

Fiscal Year	Collections Realized	Collection Ceiling		
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	$125,593,226	$132,273,000		-
2000	$141,335,631	$145,434,000		-
2001	$138,779,097	$149,273,000		-
2002	$142,000,268	$161,716,000		-
2003	$217,746,554	$222,900,000		-
2004	$246,466,405	$249,825,000		-
		Total:	**$130,077**	**$727,016**

RESERVE FOR REFUNDS AND OFFSET FOR FUTURE COLLECTIONS

The net collections exceeded the appropriations in FY's 1994 ($277), 1996 ($3,488), and 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.

Furthermore, FY 1998's collections exceeded the appropriations limit by $727,016. The requests for refunds or waivers of this amount are still pending. If the net collections still continue to exceed the appropriation limit after the requests are settled, FDA will reduce future fees to offset the surpluses. However, until the requests are settled, FDA must keep $727,016 in reserve as an offset for future collections.

RESERVE FOR FUTURE OPERATIONS

The table below provides a summary of carryover balances as of September 30, 2004, and anticipated claims on those balances. Included in those claims is also a requirement, from the congressional action on the Agency's FY 2005 appropriation, to spend $15.1 million of

the carryover funds to support a move of CDER drug review staff into the new White Oak facility in FY 2005.

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 FY 2007. The carryover amount shown as available for allocation in the table below is enough to fund estimated FY 2005 operations for approximately 1.7 months.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CARRYOVER BALANCE
As of September 30, 2004

Status of Carryover Funds	Amount
Reserve for Refunds of Excess Collections	$130,077
Reserve for Future Collection Offset	$727,016
Reserve for Move to White Oak in FY 2005	$15,092,000
Available for Allocation	$35,783,004
TOTAL Carryover Balance	$51,732,097

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 2003 and FY 2004 by organizational components. It indicates the full cost of the process for the review of human drug applications, including costs paid from both appropriations and user fee revenues. The amounts are based upon the obligations recorded as of the end of each fiscal year. In the past, over 81 percent of amounts obligated are expended within one year, and 96 percent within two 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, 2004

FDA Component	FY 2003	FY 2004
Center for Drug Evaluation and Research (CDER)	$250,370,170	$293,991,408
Center for Biologics Evaluation and Research (CBER)	$110,132,866	$91,905,443
Field Inspection and Investigation Costs (ORA)	$19,098,382	$19,646,087
Agency General and Administrative Costs (OC)	$29,840,492	$31,313,598
Total Process Cost	**$409,441,910**	**$436,856,536**
Amount from Appropriations	$209,287,410	$204,775,036
Amount from Fees	$200,154,500	$232,081,500

The costs for all components, except for CBER, rose in FY 2004. The increased expenditures primarily reflect the additional personnel hired by the organizations in FY 2004 and the mandatory pay raise for all federal employees. The reason for the decrease in CBER and the increase in CDER is because of the transfer of certain therapeutic biologics from CBER to CDER in FY 2004.

The Agency General and Administrative Costs, though up slightly from FY 2003 levels, have declined over the last 5 years as a percent of total spending on the drug review process. Only about 7 percent of drug review process costs were devoted to Agency general and administrative costs in FY 2004.

MANAGEMENT CHALLENGES FOR FY 2005

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 U. S. 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 America 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 fee structure and increased fee revenues 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.

It will be a substantial challenge both to restructure the delivery of administrative services and to consolidate information technology agency-wide. The FY 2005 Performance Plan assumes increased efficiencies through administrative reforms. If these efficiencies do not materialize as planned, FDA's ability to maintain the very high performance levels of the past several years will be challenged. Given the magnitude of the savings planned, managing the PDUFA program without compromising staffing and performance levels will be a challenge.

In FY 2005, a major PDUFA IT investment is the development of the electronic submissions gateway solution for CBER and CDER. The submissions gateway will allow both Centers to receive electronic submissions over a secure internet connection. This will enable the Centers to standardize the submission process and provide industry with a single point of entry into the FDA, as called for in the PDUFA III Electronic Applications and Submission Goals. The FDA also wants to enhance the Electronic Viewer System (EVS). This system provides the FDA reviewers with the capability of reviewing submissions in the electronic Common Technical Document (eCTD) format.

FDA will continue to be challenged by the need to hire, train, and retain qualified reviewers in FY 2005. A large number 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. The agency's ability to attract and retain the best and the brightest in medicine and science is critical to maintaining the FDA's recognized gold standard in new product safety.

Appendix A

CONDITIONS FOR ASSESSMENT AND USE OF FEES

The Food, Drug, and Cosmetic Act (the Act) specifies three major conditions that must be met each year before prescription drug user fees can 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 2004.

For making the comparisons 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 2003, the fiscal year preceding FY 2004, is 183.8. The consumer price index for April 1997 is 160.2. The result of this dividing 183.8 by 160.2 is an adjustment factor of 1.1473 for FY 2004.

The **first condition** comes from section 736(f)(1) of the Act. It states:

> Fees may not be assessed under subsection (a) 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 statement requires FDA's total Salaries and Expenses appropriation (excluding user fees) each year to be greater than or equal to FDA's FY 1997 Salaries and Expenses appropriation (excluding user fees) that multiplies 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 1.1473, an adjusted FY 1997 Salaries and Expenses Appropriation (excluding user fees, and rounded to the nearest thousand dollars) is $940,753,000.

In FY 2004, 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 $1,267,368,000. Since the FY 2004 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 user fees in FY 2004 ($249,825,000) on January 23, 2004 (Public Law 108-199). Therefore, the second condition was met.

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

> 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 1.1473, FDA's 1997 adjusted minimum spending for the human drug applications review process from appropriations (exclusive of user fees) must be $169,754,151 in FY 2004.

In FY 2004, FDA obligated $204,775,036 from appropriations for the human drug applications review process. Since $204,775,036 is greater than $169,754,151, the third condition was met.

The table below demonstrates the amounts that FDA spent on the review process of human drug applications in FY 2003 and 2004 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, 2004

	FY 1997 Adjusted for FY 2004	FY 2003	
From Appropriations	$169,754,151	$209,287,410	$204,775,036
From User Fee Revenues		$200,154,500	$232,081,500
Total Obligations		$409,441,910	$436,856,536

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 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 additional statutory exemptions in FY 1998 resulted in a loss of revenue. The increased number of exemptions required by PDUFA II reduced the number of applications that paid 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, 2004

Does not Include Data on FY 2005 Waivers Granted in FY 2004

Exempted Application Fees [1]

	FY 2000	FY 2001	FY 2002	FY 2003	FY 2004	
Orphan Product	16.3	14.5	10.0	13.5	19.5	
Pediatric Supplements	12.6	19.0	4.5			[2]
Previously Submitted			7.5	3.0	8.0	[3]
Total Exemptions	28.9	33.5	22.0	16.5	27.5	
TOTAL Value of Exemptions	**$8,250,743**	**$10,373,175**	**$6,893,040**	**$8,801,100**	**$15,771,250**	

Waived Fees

APPLICATIONS [1]

Small Business Waivers	8.3	12.0	6.0	14.3	15.3	[4]
Miscellaneous Waivers	8.3	10.3	1.0	1.0	1.0	[5]
Value of Waivers Approved	$4,714,710	$6,889,646	$2,193,240	$8,134,350	$9,319,375	

PRODUCTS

Waivers Approved	22.0	17.9	11.0	31.9	41.0
Value of Waivers Approved	$439,098	$391,867	$237,930	$1,033,560	$1,479,280

ESTABLISHMENTS

Waivers Approved	13.5	10.4	8.3	17.5	17.0
Value of Waivers Approved	$1,916,609	$1,516,242	$1,155,899	$3,673,250	$3,855,600

TOTAL VALUE--All Waivers Granted	**$7,070,417**	**$8,797,754**	**$3,587,069**	**$12,841,160**	**$14,654,255**

[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.

[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 two 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), and product license applications (PLAs), including supplements and amendments and biologic establishment license applications (ELAs) 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 agreed to phase 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 User Fee 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 parenterals approved before 9/1/92
- 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 in 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) and Supplements	CDER
Costs for the Review of Biologic License Applications (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 in FY 2004 in categories 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 categories 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 defined 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. Beginning in FY 1996, the CBER time reporting system was enhanced to collect on-line time reports for all employees for a two-week period each quarter of the year. The enhanced system reports time for 70 possible functional activities, by 10 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 four-week periods – one in each half of the fiscal year.

A similar procedure was 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 done just after PDUFA was initiated. That system collects time reports on-line from all employees other than management and administrative support personnel for a two-week period during each quarter of the fiscal year.

FDA Centers are very payroll-intensive organizations – 60 percent of all FDA funds go to pay for employee salaries and benefits, and almost all other costs are directly supporting these employees. Thus the average percent of time reported each year during this eight-week period 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 Information Technology, the Office of Management, the Office of Training and Communications, the Office of Medical Policy, the Office of Executive Programs, the Office of Information Management, and the Office of Compliance. In CBER, these components include portions of the Office of the Center Director, Office of Management, Office of Information Technology 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 percent time of all center employees in direct review and laboratory components who reported their time. Thus the average percent of time reported each year during this eight-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 being 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 2004 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 2004 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 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 2004

The time reporting systems operated by CBER and CDER indicated the 62 percent of all time spent in CBER and 79 percent of all time spent in CDER in FY 2004 was dedicated to the process for the review of human drug applications as defined in PDUFA.

FIELD INSPECTION AND INVESTIGATION COSTS

FDA's Office of Regulatory Affairs (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 the Fiscal Years 2003 and 2004.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2003 and 2004

Cost Component	FY 2003	FY 2004
Staff Years Utilized	147	147
ORA Average Salary & Benefits	$79,696	$86,376
Salary and Benefits	$11,715,260	$12,697,262
Operations, Rent and Shared Services	$7,383,122	$6,948,825
Total	**$19,098,382**	**$19,646,087**

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 Office of the Commissioner (OC). During most of FY 2004, 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 Secretary, Department of Health and Human Services. The method uses the percentage derived by dividing total Office of the Commissioner costs by the total salary obligations of the Agency, excluding the Office of the Commissioner. 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, $29,840,492 and $31,313,598 in general and administrative obligations were dedicated to the human drug review process in FY's 2003 and 2004, respectively. They are the total costs, including the funds obligated both from appropriations and user fees. The Agency general and administrative obligations in FY 2004 accounted for about 7.2 percent of the total FY 2004 costs of the human drug applications review process, which is very similar to FY 2003 (7.3 percent).