FY 1999 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

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

FEB 16 2000

The Honorable Al Gore
President of the Senate
Washington, D.C. 20510

Dear Mr. President:

Enclosed for your consideration is the annual report to Congress on the implementation of the authority and use of fees collected under the Prescription Drug User Fee Act of 1992 (PDUFA) as amended by the Food and Drug Administration Act of 1997. This financial report was prepared in accordance with section 104(b) of PDUFA and covers fiscal year (FY) 1999.

The report documents that each of the conditions specified in PDUFA for continued collection of user fees has been met and presents the user fee revenues and related obligations for 1999. Comparative data for earlier periods are also provided. In FY 99, FDA collected $126.6 million in user fees. Of that amount, $4.6 million was from previous fiscal years. FDA spent $122.5 million from PDUFA revenues, over 60 percent of which went for employee pay and benefits.

We are pleased with the success of the user fee program. Please be assured that we will continue to further strengthen and enhance our human drug application review process to expedite the availability of important medications to American consumers.

Sincerely,

Donna E. Shalala

Enclosure

Identical letters sent 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 Commerce, House of Representatives

EXECUTIVE SUMMARY

Statute requires the Food and Drug Administration (FDA) to report annually on the financial aspects of its implementation of the Prescription Drug User Fee Act of 1992 (PDUFA), as amended and extended by the Food and Drug Modernization Act of 1997 (FDAMA). This report covers fiscal year (FY) 1999.

The PDUFA, as amended, 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.

This report describes how those specific statutory conditions or "triggers" were met in FY 1999. The statements and tables included in this report also provide information on the user fee revenues and expenditures in FY 1999, and on the carryover balance. Comparative data for earlier periods is also provided.

In FY 1999, FDA collected $126.6 million in user fees and ended the year with estimated receivables of $10.6 million. The $126.6 million collected includes $122 million in FY 1999 fees and $4.6 million in fees from previous years. Most of the latter are the fees FDA received early in FY 1999 for product and establishment fees billed near the end of FY 1998.

In FY 1999, FDA spent $122.5 million from PDUFA revenues. Over 60 percent of the FY 1999 expenditures went for employee pay and benefits. Throughout FY 1999, user fees financed 909 more staff-years for the drug review process than were utilized in 1992 (before PDUFA was enacted), and 154 more FTE than the 755 FTE FDA financed from fees in FY 1998. (The FY 1998 FTE level was much lower than it otherwise would have been, however, due to concerns about funding and future revenues that arose in the second half of FY 1998.)

This infusion of human resources is the most important factor enabling FDA to meet the performance goals associated with PDUFA. The balance of the fee revenues spent in FY 1999 funded operating support for these additional employees and for investments in the Agency's infrastructure supporting the process for the review of human drug applications (including vital investments in the continued development of information technology capabilities).

Contents

BACKGROUND

PDUFA authorizes FDA to collect fees from the pharmaceutical industry to augment FDA's base resources. These additional resources are to be used to hire and support additional staff for the review of human drug applications so that effective drug products could reach the American public more quickly. PDUFA has been very successful and, with support from the pharmaceutical industry and the Administration, Congress amended and extended it through FY 2002.

Under PDUFA, as amended, an application fee must be submitted when certain new drug applications or biologic license applications are submitted. The application fee amount is set in statute, but is adjusted each year for cumulative inflation since FY 1997. In addition, FDA collects annual establishment and product fees. Under FDAMA amendments, FDA sets those fees each fiscal year so that the total revenue FDA receives from each category equals the amount FDA expects to collect from application fees. Thus, a third of the fee revenue each year comes from application fees, a third from establishment fees, and a third from product fees.

PDUFA, as amended, also requires FDA to submit two reports to Congress each fiscal year. A performance report is to be sent within 60 days of the end of the fiscal year, and a financial report is to be sent within 120 days. The FY 1999 PDUFA Performance Report, which discusses FDA's progress in meeting the goals referred to in FDAMA, was released in January 2000. This is FDA's FY 1999 PDUFA Financial Report, covering the period October 1, 1998, through September 30, 1999.

As required by statute, this report presents the legal conditions or "triggers" that must be satisfied before FDA can collect and spend the fees, and FDA's calculations showing how those conditions were met for FY 1999. This report also presents FY 1999 revenues and obligations from user fees and a summary statement of user fees by source (application, establishment, or product fees). The total costs applicable to the process for the review of human drug applications, as defined in FDAMA, are also presented, whether they were paid from fee revenues or appropriations.

In keeping with the requirements of the Chief Financial Officers Act, FDA's financial statements as of the end of each fiscal year are subject to audit by the Office of the Inspector General (OIG), Department of Health and Human Services. Beginning with financial statements for FY 1995, this audit covered all of FDA's financial systems and funds, including PDUFA revenues. The most recently completed audit is for FY 1998, and after that audit the OIG rendered an unqualified opinion on FDA's financial statements. (This is the most favorable category of auditor opinion.) The OIG audit report on FDA's FY 1999 financial statement is expected to be available later in FY 2000.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 1999

PDUFA, as amended, contains three legal conditions or "triggers" that must be satisfied each year before FDA can collect and spend user fees. FDA's calculations showing how those conditions were met for FY 1999 are summarized below and presented in more detail in Appendix A.

The first condition is that FDA's Salaries and Expenses Appropriation (excluding user fees) must meet or exceed FDA's FY 1997 Salaries and Expenses Appropriation (excluding user fees and adjusted for inflation). In FY 1999, FDA's Salaries and Expenses Appropriation (excluding user fees and excluding rent to GSA, which was also not included in the FY 1997 Appropriation amount) totaled $888,001,000. FDA's FY 1997 total Salaries and Expenses appropriation, excluding user fees, and adjusted as required by the statute, was $831,743,368. Therefore, since the FY 1999 amount is greater, the first condition was met.

The second condition is that the amount of user fees collected each year must be specifically included in appropriation Acts. For FY 1999 FDA's appropriation Acts specified that $132,273,000 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 user fees may be collected and used 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 was $147,959,689, as reported in last year's financial statement, and for FY 1999 the adjustment factor is just under 1.0144, making the adjusted amount $150,083,954. As this report shows, in FY 1999 FDA obligated $159,669,575 from appropriated funds for the review of human drug applications, which exceeds the specified minimum amount. Thus, the third condition has been met.

Appendix A provides more detail on the calculations that show that these three statutory conditions were met.

USER FEE REVENUES

The PDUFA specifies that fee revenues are to be collected from product, establishment, and application fees. Under FDAMA, application fee amounts each year are specified in statute, but adjusted for inflation. Fees for products and establishments are set each year in an attempt to make the total amount of revenue collected from each category (product fees and establishment fees) equal to the revenue FDA will collect from application fees that year.

Under PDUFA and FDAMA, any fees collected and not spent by the end of a fiscal year continue to remain available to the Agency to spend in future fiscal years. The status and claims on balances carried over from year to year are dealt with in the section on carryover balances beginning on page 6. The following table provides a breakout of user fees by fee source 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, 1999

	FY 1998	FY 1999
Fees Collected:		
Product Fees	$41,364,975	$39,188,776
Establishment Fees	$45,439,914	$40,490,948
Application Fees	$30,493,386	$42,327,063
TOTAL FEES COLLECTED:	$117,298,275	$122,006,787
Fees Receivable:		
Product Fees	$130,137	$2,956,604
Establishment Fees	$0	$2,644,605
Application Fees	$0	$0
TOTAL FEES RECEIVABLE:	$130,137	$5,601,209
Total User Fee Revenues:	$117,428,412	$127,607,996

The Fees Receivable for FY 1998 of $130,137 are all deferred collections, pending final resolution of waiver requests. Whether these actually result in collections depends on the outcome of these pending waiver requests. The Fees Receivable for FY 1999 of $5,601,209 includes $1,085,119 of deferred collections, pending final resolution of waiver requests. Most of the balance from FY 1999 is product and establishment fees billed near the end of the fiscal year.

A summary of exemption and waiver actions for FY's 1993 through 1997, 1998, and 1999 is included in Appendix B.

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 FDAMA. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C. In FY 1999, FDA continued to improve and expedite the activities involved with the process for review of human drug applications, obligating $122,515,000 of the user fees collected.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
as of September 30, 1999

Expense Category	FY 1998	FY 1999
Personnel Compensation and Benefits	$71,186,000	$75,580,000
Travel and Transportation	$2,813,000	$2,923,000
Rent	-	$5,428,000
Communications	$1,196,000	$1,322,000
Contract Services	$18,084,000	$25,210,000
Equipment and Supplies	$8,215,000	$11,949,000
Other	$121,000	$103,000
TOTAL OBLIGATIONS:	$101,615,000	$122,515,000

FDA dedicated 1,277 FTE (Full Time Equivalents or staff-years) to the review of human drug applications in FY 1992, before PDUFA was enacted. These 1,277 FTE are sometimes referred to as baseline FTE. A time reporting study was undertaken in 1993 to determine the percentage of time each division devotes to user fee related activities. This allowed calculation of FTE related costs. The percentages are updated quarterly through additional time surveys, which parallel the method used by independent consultants in FY 1993. The development of these user fee related costs associated with the review of human drug applications is described in Appendix D.

The Agency utilized and financed with user fees 909 more FTE in FY 1999 for PDUFA activities than were utilized in FY 1992. This is an increase of 154 over the 755 additional FTE fees supported in FY 1998. (Originally FDA reported 708 additional FTE in 1998, but the number should have been 755; the original report inadvertently omitted some FTE paid for in the Office of the Commissioner.) FDA's payroll costs paid from user fee funds in FY 1999 totaled $75,580,000—over 60% of the funds expended. This includes all pay and benefits for the additional 909 FTE and costs of the FY 1999 payroll increases for the baseline FTE.

A substantial amount of the remaining funds were spent on information technology (IT). FDA is engaged in an Agency-wide IT program to support the transition from a largely paper-based regulatory submission and review environment to an electronic environment. This effort is called the Electronic Regulatory Submission and Review (ERSR) program.

ERSR is comprised of a variety of projects, each of which is designed to satisfy a different part of the overall PDUFA IT goal that "the agency shall develop and update its information management infrastructure to allow, by FY 2002, the paperless receipt and processing of IND's and human drug applications...." The major ERSR project areas are described below.

- Standards and Guidance. These projects promote consistent exchange of electronic information between the Agency and external constituents. At the completion of FY 1999, several technical standards had been established and supporting guidance documents were provided to external constituents.

- Capability to Receive Electronic Submissions. These projects implement procedures and technology to support electronic submissions in lieu of paper. Progress in this area includes the establishment of Electronic Document Rooms that permit the receipt of electronic submissions in physical media format (CD-ROM, magnetic tape, etc.) from industry.

- Electronic Review. These projects enable Agency reviewers and field inspectors to conduct review activities in an electronic environment. Progress in this area includes the implementation of electronic document management systems that facilitate electronic collaboration between review staff and the expansion of existing management information systems that track the status of each review.

- Updated Infrastructure – These projects include the implementation of underlying technologies required to support the transition to a paperless review environment. Progress in this area included installing new computer hardware and software, increasing network capacity, updating the skills of technical support staff, and training for reviewers.

The total expenditure of $122,515,000 in FY 1999 is an increase of about 20% over FY 1998 amounts spent from fee revenue. However, FY 1998 expenditures from fees were sharply constrained in the final quarter of the year due to anticipated shortfalls in fee revenues. As a result, during FY 1999 FDA developed substantially scaled-back plans for expenditures over the remaining years of PDUFA—through FY 2002. The FY 1999 spending level is consistent with that scaled-back plan.

CARRYOVER BALANCES

Under PDUFA and FDAMA, any fees collected and not obligated by the end of a fiscal year continue to remain available to the Agency in future fiscal years. These revenues are referred to as carryover balances. The net result of operations in FY 1999 increased the carryover balances by $4.065.456.

The table below captures the changes in carryover balances over the course of PDUFA.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF COLLECTIONS, OBLIGATIONS, AND CARRYOVER BALANCES BY FISCAL YEAR
as of September 30, 1999

Fiscal Year	Beginning Carryover	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			

The balances above do not include estimated receivables from FY 1999 and prior years, which total $10,647,546. There are also a number of claims on these funds. Those claims (refunds, reserve for future operations, and FY 2000 operating needs) are explained below. As a result of these claims, we expect a reduction in the carryover balance at the end of FY 2000.

COLLECTION CEILINGS AND POTENTIAL REFUNDS AND OFFSETS

PDUFA prohibits the Agency 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 will be refunded. Under FDAMA, balances collected in excess of amounts specified in appropriations after FY 1997 may be kept, and used to reduce fee charges that would otherwise be made in a later fiscal year. The following table depicts collections since FY 1993, collection ceilings specified in appropriations, and amounts to be either refunded or used to offset future collections.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF FEES COLLECTED, COLLECTION CEILINGS, AND POTENTIAL REFUNDS
as of September 30, 1999

Fiscal Year	Collections Realized	Collection Ceiling	Potential Refund	Potential Offset to Future Collections
1993	$35,973,490	$36,000,000	-	
1994	$56,481,650	$56,284,000	$197,650	
1995	$77,783,800	$79,423,000	-	
1996	$86,602,685	$84,723,000	$1,879,685	
1997	$91,873,176	$87,528,000	$4,345,176	
1998	$117,298,275	$117,122,000		$176,275
1999	$122,006,787	$132,273,000		-
Total:			**$6,422,511**	**$176,275**

As of September 30, 1999, collections have exceeded appropriations in FY's 1994 ($197,650), 1996 ($1,879,685) and 1997 ($4,345,176). A total of $6,422,511 will have to be refunded, decreasing the carryover balance. The amount to be refunded for FY 1997 is likely to increase because a second-half application fee will be paid for this year. Any surplus collections will be accumulated by the Agency until (1) further collections of fees from each fiscal year are unlikely and (2) all waivers and refunds have been settled. Most of the waivers and refund requests for prior years that were pending at the beginning of FY 1999 have now been settled. Completing work on the few remaining will be a priority in FY 2000.

When all outstanding waiver requests for years prior to FY 1998 are resolved, it is FDA's intention to refund the total amount in proportion to the total fees paid (application, establishment, and product fees combined) by each firm for the specific fiscal year to which the refund applies.

RESERVE FOR FUTURE OPERATIONS

A substantial carryover balance is necessary at the end of each fiscal year to ensure adequate operating funds in the first 4 months of each new fiscal year. Each year, two-thirds of the PDUFA fees (product and establishment fees) are not paid to FDA until January 31--4 months after the fiscal year starts. The other one-third (application fees) is spread out over the year. For estimation purposes, this portion is distributed evenly over 12 months. These application fees in aggregate would cover FDA costs for 1.3 of the first 4 months of the fiscal year. FDA needs to carry forward, as a bare minimum, at least 2.7 months of operating costs into each new fiscal year to cover expenses until the product and establishment fees are received on January 31. As shown in FDA's PDUFA II Five-Year

Plan, at the end of FY 2000 the Agency needs to carry forward a minimum of $31.8 million to cover essential future operating costs.

Reserve for Refunds of Fees Paid but still Pending Waiver Resolution

As reflected in Appendix B, there are waivers pending for a total of $3,982,641. If all of these waivers are granted, FDA will have to refund this amount of fees already paid, so FDA has a pending liability for this amount.

Amount Allocated in FY 2000

In addition to the items discussed above, at least $7.5 million from carryover balances will be allocated to FDA components in FY 2000, as reflected in the most recent update of FDA's PDUFA II Five-Year Plan. In addition, $18 million planned and allocated to the centers in FY 1999 were not obligated as of September 30, 1999. This $18 million will also be reallocated in FY 2000, for a total of $25.5 million.

Food and Drug Administration
Summary Statement of Claims on Carryover Balance
as of September 30, 1999

Nature of Claim	Amount
Reserve for Refunds	$6,422,511
Future Collection Offset	$176,275
Minimum Reserve for Future Operations	$31,827,000
Reserve for Pending Waiver Requests	$3,982,641
Amount Allocated in FY 2000	$25,500,000
TOTAL CLAIMS	$67,908,427

The chart above summarizes all the claims on the carryover balance.

Summary of Receivables and Payments Deferred

At the end of FY 1999, in addition to the cash collected, FDA had receivables totaling $10,647,546. Of this amount, a total of $5,917,410 has been deferred and will not be payable until a final decision is made on pending waiver requests. If all of these waiver requests are granted, then none of this $5,917,410 will materialize as fee payments. Accordingly, a reserve of $5,917,410 has been established within accounts receivable for losses, waivers, and refunds. The balance, exclusive of this reserve, is $4,730,136.

Originally under PDUFA there was no limitation on when waivers or refunds could be requested. That has been remedied by FDAMA. No further waiver or refund requests may be made for applications submitted through FY 1998. The agency is actively working on resolving all pending waiver or refund requests.

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's 1998 and 1999 by organizational component. This presents 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 obligations recorded as of the end of each fiscal year. 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 COST
as of September 30, 1999
(numbers may not add due to rounding)

FDA Component	FY 1998	FY 1999
Center for Drug Evaluation and Research (CDER)	$144,227,003	$166,562,594
Center for Biologics Evaluation and Research (CBER)	$66,275,840	$73,316,714
Field Inspection and Investigational Costs (ORA)	$16,904,301	$17,753,152
Agency General and Administrative Costs	$26,044,491	$24,552,117
Total Process Costs	**$253,451,635**	**$282,184,575**
Amount from Appropriations	$151,836,635	$159,669,575
Amount from Fees	$101,615,000	$122,515,000

The costs for CDER rose significantly in FY 1999. This reflects: (1) increased staffing levels as a result of more aggressive and successful recruiting; and (2) increased information technology expenditures as CDER gears up for the new challenges imposed by PDUFA goals for FY's 1998-2002.

CBER expenditures didn't increase as rapidly as CDER's, in spite of substantial increases in personnel costs in FY 1999, because research resources that had been allocated to CBER from PDUFA revenues are being phased out and offset review staff increases. CBER increased its information technology expenditures as well.

The slight increases in ORA costs is roughly proportional to the increase in overall process costs.

The decrease in Office of the Commissioner costs, while all program costs were increasing, results directly from the reorganization and downsizing of the Office of the Commissioner completed in 1999.

MANAGEMENT CHALLENGES FOR FY 2000

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. In FY 2000, FDA will be challenged to sustain these improvements and meet increasingly difficult PDUFA performance goals while resources for most other programs are dwindling.

Assuring that enough appropriated funds are spent on the process for the review of human drug applications to meet requirements of PDUFA, and at the same time spending our resources in a way that best protects the health and safety of the American people is becoming increasingly difficult. Each year, the amount that FDA must spend on the drug review process is increased by an inflation factor. Yet since 1992 FDA has not received increased appropriations to cover the costs of the across-the-board pay increases that must be given to all employees.

The result is that our workforce and real resources for most programs other than PDUFA have contracted each year since 1992 while we struggle to assure that enough funds are spent on the drug review process to meet the PDUFA trigger. Several consecutive years of operating in this way have made it difficult to continue to further reduce staffing levels in FDA programs other than drug review. We are increasingly concerned that spending enough budget authority on the drug review process to meet the statutory conditions makes FDA less able to manage the resources available in a way that best protects the public health and merits public confidence. Examples of areas we have not been able to fund adequately include responding to reports of adverse events related to the use of prescription drugs.

In FY 2000 FDA will continue working toward the goal of receiving applications electronically by the end of FY 2002. This major change in how FDA does business should provide significant savings to industry. Setting standards and sequencing the development and implementation of the necessary infrastructure to achieve this goal demands careful planning, vigilance with respect to newly emerging technologies, and constant monitoring.

Additionally, in FY 2000 FDA will continue to be challenged by the need to hire and train qualified reviewers. FDA's experienced reviewers are in demand and have excellent employment opportunities. The Agency continued to experience review staff attrition of about 10 per cent in FY 1999. Recruiting and training new staff is a constant challenge.

Finally, the Agency continues to struggle to anticipate and fully understand the new technologies that are fundamental to many new therapies. Understanding these new technologies (especially biotechnologies) is essential to expeditious review of many new products. Since support of PDUFA related research from fee revenues is being phased out, the Agency is increasingly dependent on appropriated funds to sustain its scientific knowledge base in emerging areas such as gene and cell therapy.

Appendix A

CONDITIONS FOR ASSESSMENT AND USE OF FEES

The Food, Drug and Cosmetic Act (the Act), as amended by PDUFA and FDAMA, specifies three major conditions that must be met each year before user fees can be collected and spent. A summary of these conditions and how they were met was provided earlier on page 2. A more detailed presentation of each of these conditions is provided below, along with an explanation of how the condition was met in FY 1999.

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 requires that FDA's total Salaries and Expenses appropriation (excluding user fees) each year must be greater than or equal to FDA's FY 1997 Salaries and Expenses appropriation (excluding user fees). For making this comparison, FDA's 1997 Salaries and Expenses appropriation must be adjusted each year by a factor, which is defined in section 735(8) of the Act. It states:

> The term 'adjustment factor' applicable to a fiscal year is the lower of-
>
> (A) 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, or
>
> (B) the total of discretionary budget authority provided for programs in the domestic category for the immediately preceding fiscal year (as reported in the Office of Management and Budget sequestration preview report, if available, required under section 254(c) of the Balanced Budget and Emergency Deficit Control Act of 1985) divided by such budget authority for fiscal year 1997 (as reported in the Office of Management and Budget final sequestration report submitted after the end of the 105th Congress, 1st Session).

The first calculated factor is the consumer price index of April 1998 (162.5), which is the fiscal year immediately preceding FY 1999, divided by the consumer price index for April 1997 (160.2). The result of this division is a factor of 1.0144.

The second calculated factor is the domestic discretionary budget authority for FY 1998 ($284.1billion), the fiscal year immediately preceding FY 1999, as reported in the final sequestration report submitted after the end of the 105th Congress, 2nd Session, divided by the domestic discretionary budget authority for FY 1997, as reported in the final sequestration report submitted after the end of the 105th Congress. 1st Session ($253.5 billion). The result of this division is a factor of 1.1207.

The lower of these two numbers is the first factor, 1.0144. Accordingly, the adjustment factor to be used for FY 1999 is 1.0144.

FDA's total FY 1997 Salaries and Expenses appropriation, excluding fees, was $819,971,000. Multiplying this amount by the adjustment factor of 1.0144 results in an adjusted Salaries and Expense Appropriation minimum, excluding fees, of $831,743,368.

For FY 1999, 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 $888,001,000. Since the FY 1999 amount exceeds the FY 1997 adjusted amount, the first condition was met.

The **second condition** comes from Section 736(g)(2)(A). It states that fees "shall be collected in each fiscal year in an amount specified in appropriation acts, or otherwise made available for obligation, for such fiscal year...." Without a specific appropriation, no fees may be collected.

The appropriation Act (Public Law 105-277) specifying amounts collectable from fees during FY 1999 was signed by the President on October 21, 1998. It provided $132,273,000 to come from fees collected. Thus, the second condition was met, and fees may be collected.

The **third condition** in the Act, in Section 736 (g) (2) (B), 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 obligations for the process for the review 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 1.0144 derived above, FDA's 1997 adjusted costs for the process for the review of human drug applications paid from appropriations exclusive of fees, is $150,083,954.

The following table shows the FDA costs (obligations) for the process for the review of human drug applications for FY's 1998 and 1999, and the adjusted FY 1997 amount from appropriations. It also shows the amount of these costs that was charged to appropriations and the amount met from user fee revenues. Since the FY 1999 amount spent from base appropriations exceeded the FY 1997 adjusted amount, the third condition was met.

FOOD AND DRUG ADMINISTRATION
OBLIGATIONS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
as of September 30, 1999

	Adjusted FY 1997	FY 1998	FY 1999
From Appropriations	$150,083,954	$151,836,635	$159,669,575
From User Fee Revenues		$101,615,000	$122,515,000
Total Obligations		$253,451,635	$282,184,575

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 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 FDAMA new exemptions from fees have been added beginning in FY 1998. These specific exemptions are automatic and do not require a waiver request. They include:

- human drug applications 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.

Beginning in FY 1998, FDAMA also provides 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 could be granted a small business exception.

The additional statutory exemptions in FY 1998 resulted in a substantial loss of revenue, as can be seen at the top of the chart on the next page. The increased number of exemptions required by FDAMA amendments reduced the number of applications that paid fees.

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

During the past year, most of the pre-1998 requests for waivers on the basis that fees paid exceeded costs FDA incurred were resolved. Fewer than 5 of these old claims remain to be resolved. The tables on the following page summarize the exemption and waiver actions taken by FDA for fees payable in FY's 1993 through 1997, and 1998 and 1999, and pending waiver requests for fees payable from the same periods.

EXEMPTIONS AND WAIVERS

(Exemptions counted in Full Application Equivalents)

Exemptions	FY 1993 Through FY 1997	FY 1998	FY 1999
APPLICATIONS			
Exemptions Provided			
Orphan Product	Treated as Waivers	16	12.5
Pediatric Supplements	Treated as Waivers	8	5.25
Small Business	18	15	7
Total Exemptions	18	42	24.75
TOTAL VALUE	**$3,272,000**	**$10,659,109**	**$6,738,980**

Approved Waivers

APPLICATIONS			
Waivers Approved	74	4	1
Value of Waivers Approved	$11,035,875	$1,027,394	$272,282
PRODUCTS:			
Waivers Approved	261	51	14
Value of Waivers Approved	$3,003,600	$910,959	$220,368
ESTABLISHMENTS:			
Waivers Approved	65	20	7
Value of Waivers Approved	$7,471,500	$2,329,436	$899,045
TOTAL VALUE	**$21,510,975**	**$4,267,789**	**$1,391,695**

Pending Waivers (Fees Already Received)

APPLICATIONS:			
Waivers Pending	3	0	4
Allowance for Pending Waivers	$333,150	$0	$884,917
PRODUCTS:			
Waivers Pending	10	4	19
Allowance for Pending Waivers	$260,350	$74,364	$413,608
ESTABLISHMENTS:			
Waivers Pending	4	3	9
Allowance for Pending Waivers	$582,150	$291,030	$1,143,072
TOTAL VALUE	**$1,175,650**	**$365,394**	**$2,441,597**

Pending Waivers (Payments Deferred)

APPLICATIONS:			
Waivers Pending	3	0	0
Allowance for Pending Waivers	$152,500	$0	$0
PRODUCTS:			
Waivers Pending	17	1	13
Allowance for Pending Waivers	$201,200	$18,591	$238,732
ESTABLISHMENTS:			
Waivers Pending	36	0	7
Allowance for Pending Waivers	$4,460,000	$0	$846,387
TOTAL VALUE	**$4,813,700**	**$18,591**	**$1,085,119**

Appendix C

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

The PDUFA, as amended by the FDAMA and the related PDUFA House of Representatives Report 102-895 ("House Report"), defines the process for the review of human drug applications and the costs which may be included in that process. Using these definitions (and further refinements as necessary) 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 (NDA's), biologic license applications (BLA's), and product license applications (PLA's), including supplements and amendments and biologic establishment license applications (ELA's) 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 FDAMA FDA agreed to phase out research supported by fee revenues

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 Food and Drug Administration, 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 Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER), 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), Product License Applications (PLA's), Establishment License Applications (ELA's) and Supplements	CBER
Field Inspection and Investigation Costs	ORA
Agency General and Administrative Costs	OC

The costs were accumulated using a variety of methods including time reporting, management surveys, and detailed interviews. 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 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 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) review and laboratory components; 2) indirect

review and support components; and 3) user fee excluded components. Costs are accumulated by cost centers. The allocation of costs for the three categories and center-wide expenses are discussed below.

Review and Laboratory Components:

The review and laboratory components, as organized during FY 1999, have the primary responsibility for the review of human drug applications and supplements. Below is a list of these direct review and laboratory components in CDER and CBER.

REVIEW AND LABORATORY COMPONENTS

CDER	CBER
Office of the Center Director	Office of the Center Director
Office of Medical Policy	Veterinary Services
Division of Drug Marketing, Advertisement, and Communications	Regulations and Policy Staff
Office of Post Marketing Drug Assessment	Office of Review Services
Division of Drug Risk Evaluation I	Biostatistics and Epidemiology
Division of Drug Risk Evaluation II	Office of Blood Research and Review
Office of Drug Evaluation I	Transfusion Transmitted Diseases
Neuropharamacological Drug Products	Hematology
Oncologic Drug Products	Blood Applications
Cardio-Renal Drug Products	Office of Therapeutics Research and Review
Office of Drug Evaluation II	Cellular and Gene Therapies
Metabolic and Endocrine Drug Products	Hematologic Products
Pulmonary Drug Products	Monoclonal Antibodies
Anesthetic, Critical Care and Addiction Drug Products	Clinical Trial Design and Analysis
Office of Drug Evaluation III	Application Review and Policy
Gastro-Intestinal and Coagulation Drug Products	Cytokine Biology
Reproductive and Urologic Drug Products	Office of Vaccines Research and Review
Medical Imaging and Radiopharmaceutical Drug Products	Bacterial Products
Office of Drug Evaluation IV	Viral Products
Anti-Viral Drug Products	Vaccines and Related Product Applications
Anti-Infective Drug Products	Allergenic Products and Parasitology
Special Pathogens and Immunodulatory Drug Products	Office of Compliance and Biologics Quality
Office of Drug Evaluation V	Manufacturing and Product Quality
Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products	Advertising and Promotional Labeling Staff
Dermatologic and Dental Drug Products	
Over-the-Counter Drug Products	
Office of Biostatistics	
Quantitative Methods and Research Staff	
Biometrics I, II, and III	
Office of Pharmaceutical Science	
Office of New Drug Chemistry	
Office of Clinical Pharmacology and Biopharmaceutics	

A total time reporting study was conducted from July 18, 1993, to November 6, 1993, as part of a contract with Arthur Andersen & Company, to measure the level of user fee related costs for each of the CBER and CDER review components. Over 1,000 staff participated in the 16-week study. The time sheets were designed to capture information on activities based on the definitions for the process for the review of human drug applications in the Act. Using the results of the time reporting study, a user fee related percentage was calculated for each participating division and applied to the total FY 1992 costs for each division to determine its costs for the process for the review of human drug applications.

The results of the 16-week time reporting exercise are representative of the activities during FY's 1992, 1993, and 1994 in CDER, and were used to calculate process costs for CDER each year. The results of the Arthur Andersen & Company 16-week total time reporting study were used to measure CBER's FY 1993 user fee costs. A pre-existing CBER workload measurement procedure, which was validated by the results of the Arthur Andersen study, was used to measure CBER's FY 1992 and FY 1994 user fee costs.

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, Office of Information Technology, the Office of Management, the Office of Training and Communications, the Office of Medical Policy, and the Office of Compliance. In CBER, these components include portions of the Office of the Center Director, Office of Management, and the Office of Communications, Training, and Manufacturers Assistance.

In CDER, detailed interviews were conducted with the division directors or their designees for each of the divisions classified as indirect review and support for the human drug review process. The first step of the interviews was to identify the activities in the division and classify these as user fee related or user fee excluded activities based on the definitions in the Act. Then, using information provided by the division directors, the number of full time equivalent (FTE) employees involved in these activities was estimated. With this information, an overall user fee applicable percentage was calculated for each division.

In CBER, the workload measurement procedures were used to measure the level of effort of user fee related activities in the compliance divisions. Most of the Office of the Center Director, Office of Management, and the Office of Communications, Training, and Manufacturers Assistance are considered support organizations to CBER, therefore a percent of their time is added to each activity.

User Fee Excluded Components

Based on a review of a component's activities and the definitions in the Act, some organizations within the centers were completely excluded from the calculation of

costs related to the process for the review of drug applications. An example of a user fee excluded component is the Office of Generic Drugs in CDER. In CBER, all cost centers perform some PDUFA work, although it can be as little as 5 percent.

Center-wide Expenses

A number of center-wide expenses are collected in central accounts rather than being charged directly to a specific division. These costs include rent, utilities, some computer equipment, facilities repair and maintenance, and extramural and service contracts. Many of these costs could be traced back to the specific division that generated the cost and were assigned the user fee related 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.

CENTER TIME REPORTING ENHANCEMENTS

In May 1995, CDER conducted an internal time reporting study of all CDER units previously surveyed by Arthur Andersen in 1993. This internal study enabled CDER to update user fee percentages on a one-time basis. In FY 1996, CDER implemented quarterly on-line time reporting. These quarterly updates facilitated timely reporting of user fee percentages by the various components of the Center.

In FY 1995, CBER began quarterly collection of actual hours worked reported over a 2-3 consecutive week period. Time was reported for 43 functional activities, by 9 product classes. Research time was reported for specific numbered research projects. These quarterly surveys were used to calculate the percent of CBER staff time expended for PDUFA work in each component for each reporting period. That percentage was then applied to the total quarter's costs of that component to calculate its total expenditures for the process of reviewing human drug applications. By mid-1995, CBER had begun a pilot computer-based reporting system (mirroring the paper submissions), that was accessed through the network (paperless.) By the end of the fiscal year, CBER designed, with the assistance of Arthur Andersen, an on-line reporting system called the "Resource Reporting System", that made it easier for employees to report and provide more data to management.

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. This new survey captures the expenditure of time on PDUFA-related activities and other CDER mission-oriented activities for a two-week period during each quarter, just as is done in CBER.

CENTER RESEARCH COVERED BY THE PRESCRIPTION DRUG USER FEE ACT

The research activities described in this section were included when FDA originally calculated base costs for the process for the review of human drug applications for FY 1992. Under PDUFA, 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 the extension of PDUFA, FDA agreed to phase out the use of fee revenues to support these research costs. The phase-out is to be completed by FY 2002. After the phase-out of fee revenues supporting this research, FDA expects the remaining research to continue to be supported by appropriated funds, just as it was prior to FY 1993.

The FDA performs research to determine the risks and benefits of pharmaceutical agents and to set appropriate standards and methods for analysis. These activities include research on specific products or product classes that are approved or under review. Research is carried out in biomedical areas to develop expertise necessary to address new technologies, issues and emerging areas, develop and validate testing methodologies, and to establish drug and biologic standards. All of these activities are fundamental to the evaluation of human drugs and biological products. Research activities that directly support the process for the review of drug and biologic applications are described below.

Laboratory activities that are included in the drug review process also include activities necessary for the analysis and release of individual lots of biologic products (under section 351 of the Public Health Service Act) and development and validation of assays to ensure batch-to-batch consistency and reliability.

FDA defined research activities associated with the review of new drugs and biologics such as research to: (1) facilitate review of clinical and product testing, (2) support policy development, (3) validate assays, and (4) develop standards. These research activities are focused on approved products or product classes, or products or product classes under review or investigation.

Laboratory activities <u>not</u> considered a part of the process for the review of human drug application as defined in PDUFA include laboratory work associated with generic drugs, over-the-counter monographs, allergenic extracts, in-vitro diagnostics, whole blood or blood components, or large volume parenterals approved prior to September 1, 1992.

<u>Types of Research</u>
User fee related research is categorized based on its impact on the drug approval process:

> <u>Review of the Manufacturing Process</u>
> The evaluation of new biological and drug products requires a careful review of the manufacturing process. The process of manufacture can potentially result in subtle changes in the product characteristics that could affect safety and efficacy of the

product. This review is especially critical in the evaluation of new products manufactured using new technologies.

Development and Validation of Test Methodologies
Standards for testing must be set for each drug or biologic product in order to ensure its identity, purity, and potency prior to approval. Frequently, test methods are developed and validated in FDA laboratories. These tests are used for biologic lot release and for characterizing qualification lots of products submitted for approval.

Safety and Toxicity
New drugs and biological products are evaluated for safety and toxicity. Frequently, a product will represent a new class whose toxicity profile is not well established. In these cases, it may be necessary for FDA to conduct studies to gain information in order to establish policy and safety standards for similar products in the new class.

Pharmacology
The pharmacology of drugs and biological products must be understood in order to evaluate potential toxicities and measures of potency. In some cases a detailed understanding of the mechanisms of action, metabolism, distribution, and excretion is critical to establish tests for potency and to better understand toxicity. It may also be necessary for pharmacodynamic endpoints to establish appropriate product dosing and to develop in-vivo and in-vitro standards for evaluating manufacturing changes.

Clinical
The study of drugs and biological products in human subjects is an important component of FDA research. Many important questions related to the optimal use of a given drug in human subjects or patients may not be part of the standard drug development process. However, such data would facilitate optimal use of the product. Further, some of these research questions impact on regulatory review policy for the product class being studied. Examples of such research include the study of drugs in special populations (e.g. women, the elderly, patients with renal or hepatic impairment), evaluation of drug interactions and the development of pharmacokinetic/pharmacodynamic correlations, or safety of combination vaccines.

FIELD INSPECTION AND INVESTIGATION COSTS

Most field inspection and investigation costs are incurred by FDA's Office of Regulatory Affairs (ORA). ORA costs are incurred in both district offices (the "field") and headquarters support offices. The Agency has accumulated ORA costs through the use of the Program Oriented Data System (PODs). PODs is a time 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 PODs 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 for the FY's 1998 and 1999, respectively.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
as of September 30, 1999

Cost Component	FY 1998	FY 1999
Staff Years Utilized	180	168
ORA Average Salary	$64,680	$66,990
Salary and Benefits	$11,642,314	$11,254,272
Operations and Rent	$5,261,987	$6,498,879
Total	**$16,904,301**	**$17,753,151**

AGENCY GENERAL AND ADMINISTRATIVE COSTS

The Agency general and administrative costs are incurred in the FDA's Office of the Commissioner (OC). OC is comprised of the following offices:

- Immediate Office of the Commissioner
- Office of the Senior Associate Commissioner
- Office of Policy, Planning and Legislation
- Office of International and Constituent Relations
- Office of Management and Systems

The OC costs applicable to the process for the review of human drugs 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 drugs in CDER, CBER, and ORA to arrive at the total General and Administrative Costs.

Using this process, $26,044,491 and $24,552,117 in general and administrative obligations were dedicated to the human drug review process in FY's 1998 and 1999, respectively. Although the costs applicable to the process have increased in FY 1999, the Agency general and administrative costs have decreased, largely due to the Commissioner's reorganization that moved a number of functions out of the Office of the Commissioner and into the centers. As a result, in FY 1999 general and administrative obligations accounted for only 8.7 percent of the total FY 1999 cost of the process for the review of human drug applications. This is a reduction from 11.1 percent in 1993, the first year operating under PDUFA.