FY 2003 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 2004

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

March 24, 2004

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 the Congress required by the Prescription Drug User Fee Act of 1992 (PDUFA), as amended. This is the first financial report under PDUFA III, which authorizes higher levels of fee revenue to support the drug approval process. This report covers fiscal year (FY) 2003, documenting how each of the conditions specified in PDUFA for continued collection of prescription drug user fees was met.

The report also presents the user fee revenues and related expenses for FY 2003 and comparative data for earlier periods, and details the amounts carried over at the end of each year that remain available. For FY 2003, FDA collected $210 million in user fees, and spent $200 million. Almost 60 percent of the fee revenue was spent for salaries and benefits. This infusion of human resources is the single most critical factor enabling FDA to meet the performance goals associated with PDUFA—goals that become increasingly more stringent each year.

Sincerely,

/s/

Tommy Thompson

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) to report annually on the financial aspects of its implementation of the Prescription Drug User Fee Act of 1992 (PDUFA), as amended. This report, covering fiscal year (FY) 2003, is the first report that issued since the enactment of the Prescription Drug User Fee Amendments of 2002 (PDUFA III).

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 those specific statutory conditions or "triggers" were met in FY 2003. The statements and tables included in this report also provide information on the user fee revenues and expenditures in FY 2003, and on the carryover balance. Comparative data for earlier periods are also provided.

For FY 2003, FDA collected $210 million in fees. FDA also had receivables of $6 million. At the beginning of the year FDA had projected collecting $222.9 million, but fewer fee-paying applications than projected were received in FY 2003. This realization of less revenue than projected is not an indication that the overall FDA review workload has declined—only that an increasing number of industry submissions were in categories for which fees were not paid.

In FY 2003, FDA spent $200 million from PDUFA revenues—about $10 million less than net collections for the year, increasing the balance of funds collected and appropriated in previous years, and still available for obligation, to $32 million at the end of FY 2003.

Challenges facing FDA in FY 2004 include hiring and training additional staff to meet the PDUFA III goals, even though spending under terms of a series of continuing resolutions delayed the hiring of additional staff by almost four months.

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BACKGROUND

PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment appropriations spent on drug review. These additional resources were to be used to hire and support additional staff for the review of human drug applications so that safe and effective drug products reach the American public more quickly. PDUFA was very successful and, with support from the pharmaceutical industry, other stakeholders, and the Administration, Congress amended and extended it through FY 2007 (PDUFA III).

Under PDUFA III one third of the fee revenue each year comes from application fees, a third from establishment fees, and a third from product fees. An application fee must be submitted when certain new drug applications (NDA's) or biologic license applications (BLA's) are submitted, and product and establishment fees are due annually on October 1. The total revenue amounts to be derived each year from each category—application fees, product fees, and establishment fees—are set by statute. Those statutory amounts are then adjusted each year both for cumulative inflation since FY 2003 and for changes in drug review workload. PDUFA III authorizes FDA to set fees each fiscal year so that the total revenue FDA receives from each category equals the statutory amount after adjustment for inflation and 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 of the end of the fiscal year, and a financial report is to be sent within 120 days. The FY 2003 PDUFA Performance Report, which discusses FDA's progress in meeting the goals referred to in PDUFA III, is being separately transmitted to Congress. This is FDA's FY 2003 PDUFA Financial Report, covering the period October 1, 2002 through September 30, 2003.

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 2003. This report also presents FY 2003 revenues and obligations from user fees and a summary statement of user fees by source (application, establishment, or product fees). The total costs of the process for the review of human drug applications, as defined in PDUFA III, are also presented—both the costs paid from fee revenues and the costs paid from appropriations.

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 2003. This is the most favorable category of audit opinion.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 2003

PDUFA III 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 2003 are summarized below and presented in more detail in Appendix A.

The first condition is that FDA's overall Salaries and Expenses Appropriation (excluding user fees) must meet or exceed FDA's overall FY 1997 Salaries and Expenses Appropriation (excluding user fees and adjusted for inflation). In FY 2003, 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 $1,268,098,000. FDA's FY 1997 total Salaries and Expenses appropriation, excluding user fees, and adjusted as required by the statute, was $920,253,453. Therefore, since the FY 2003 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 2003, FDA's Appropriation Act specified that $222,900,000 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, adjusted for inflation, is $166,055,159. In FY 2003, FDA obligated $209,287,410 from appropriated funds for the review of human drug applications. Since this amount exceeds the specified minimum amount, 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

PDUFA III specifies that fee revenues are to be collected from establishment, product, and application fees. The statute specifies revenue amounts for each of these fee categories, and that these revenue amounts are to be adjusted each year for inflation and workload. Fees for each category are set each year so that the total amount of revenue collected from each category (application fees, establishment fees, and product fees) equals the statutory revenue target as adjusted for inflation and workload.

Under PDUFA, any fees collected and appropriated but not spent by the end of a fiscal year continue to remain available to FDA to spend in future fiscal years. The balances carried over from year to year are covered 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, 2003

	FY 2002	FY 2003
Fees Collected:		
Product Fees	$50,420,578	$69,012,000
Establishment Fees	$51,250,146	$74,399,534
Application Fees	$40,329,544	$65,959,471
TOTAL FEES COLLECTED:	**$142,000,268**	**$209,371,005**
Fees Receivable:		
Product Fees	$43,260	$2,595,698
Establishment Fees	$70,055	$3,362,587
Application Fees	$0	$0
TOTAL FEES RECEIVABLE:	**$113,315**	**$5,958,285**
Total User Fee Revenues:	**$142,113,583**	**$215,329,290**

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 2002, even if it is received in FY 2003, is attributed to FY 2002 revenues. Totals reported for each year are net of any refunds for that year.

The Fees Receivable for FY 2002 of $113,315 are all deferred collections, pending final resolution of waiver requests. Most of the FY 2003 accounts receivable are product and establishment fees billed near the end of the fiscal year. Fees receivable for FY 2003 also include deferred collections of $573,789 pending final resolution of waiver requests. A summary of exemption and waiver actions 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 PDUFA III. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C. In FY 2003, FDA obligated $200,154,500 from user fee revenues.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
As of September 30, 2002 and 2003

Expense Category	FY 2002	FY 2003
Personnel Compensation and Benefits	$112,852,095	$130,939,056
Travel and Transportation	$3,834,105	$4,527,825
Rent	$1,040,000	$8,719,000
Communications	$1,288,359	$1,284,635
Contract Services	$31,834,035	$43,500,289
Equipment and Supplies	$10,539,764	$10,246,121
Other	$423,742	$937,574
TOTAL OBLIGATIONS:	$161,812,100	$200,154,500

FDA dedicated 1,277 staff-years to the review of human drug applications in FY 1992, before PDUFA was enacted. 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 personnel related costs. The percentages are updated regularly 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 more detail in Appendix D.

In FY 2003, PDUFA fees and appropriations paid for 1,201 more staff years than were used in 1992 for the process for the review of human drug applications. FDA's payroll costs paid from user fee funds in FY 2003 represented almost 60 percent of the funds expended. This includes all pay and benefits for the additional personnel.

A large percentage of the remaining funds were used to support information technology (IT) investments. FDA continues to transition from a largely paper-based regulatory submission and review environment to an electronic environment through the Electronic Regulatory Submission and Review (ERSR) program. The ERSR program is described in the PDUFA III IT Five-Year Plan. In addition, Section XII of the PDUFA III goals letter, signed by the Secretary on June 4, 2002, describes the Electronic Applications and Submission Goals, also referred to as the PDUFA IT goals. These goals, in summary, require the FDA to:

a) Centralize accountability and funding for all PDUFA IT initiatives/activities under the Agency Chief Information Officer (CIO);
b) Hold quarterly briefings with Industry and provide annual progress reports to FDA Commissioner;

c) Ensure common solutions for secure exchange and submission of application components;
d) Provide a single point of entry for FDA for all electronic submissions within a highly secure environment;
e) Implement the electronic common technical document (eCTD), which is a common format for electronic submissions in support of marketing applications to be used worldwide. It is developed under the auspices of the International Conference on Harmonization. The Agency must provide format specifications for eCTD's;
f) Conduct an objective analysis for consolidation of PDUFA III IT infrastructure and desktop management services;
g) Implement a software development process improvement initiative consistent with the concepts and requirements provided by the Capability Maturity Model (CMM) framework;
h) Ensure that PDUFA organizations use the same software applications (e. g., eCTD, COTS) for common business needs where appropriate; and
i) Publish a PDUFA III 5-year Plan within 6 months of authorization.

As stated in the PDUFA IT Five-Year Plan, "FDA considers the first year of the PDUFA III timeframe to be a period of considerable transition." Given this background, over the first year of PDUFA III the FDA has made significant progress in addressing the PDUFA IT goals. In this first year, working with each of the FDA organizations that plays a role in PDUFA, the FDA CIO has established the PDUFA IT investment governance process, allowing the FDA to:

- Review, prioritize and fund new PDUFA investments
- Review and authorize adjustment to existing PDUFA investments
- Review and authorize PDUFA maintenance and operations funding, and
- Maintain and update the PDUFA IT 5-Year Plan to ensure linkage to Agency strategic goals.

Major accomplishments of FY 2003 include: the initial production release of the eCTD software; the establishment of an Agency Project Management Office; and the establishment of the IT Shared Services organization to address the infrastructure consolidation requirements.

CARRYOVER BALANCES

Under PDUFA any 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 2003 increased the carryover balances by $9,512,551.

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 September 30, 2003

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	$22,683,225	$209,667,051	$200,154,500	$32,195,776
2004	$32,195,776			

The balances above reflect cumulative cash at the beginning/end of each fiscal year, and net cash collected during each fiscal year for all cohort years. The figures do not include accounts receivable. The net collections balance shown above for FY 2003 of $209,667,051 is a little more than the FY 2003 collections balance on page 3 of $209,371,005. Most of this difference is the result of collections during FY 2003 of amounts applicable to earlier cohort years.

There are also a number of claims on these carryover funds. Those 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 net collections since FY 1993, collection ceilings specified in appropriations, and amounts that may 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, 2003

Fiscal Year	Collections Realized	Collection Ceiling	Potential Refund	Potential Offset to Future Collections
1993	$35,973,500	$36,000,000	-	
1994	$56,284,277	$56,284,000	$277	
1995	$77,498,800	$79,423,000	-	
1996	$84,726,488	$84,723,000	$3,488	
1997	$87,654,312	$87,528,000	$126,312	
1998	$117,849,016	$117,122,000		$727,016
1999	$125,593,226	$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	$209,371,005	$222,900,000		
		Total:	**$130,077**	**$727,016**

RESERVE FOR REFUNDS AND OFFSET FOR FUTURE COLLECTIONS

As of September 30, 2003, collections have exceeded appropriations in FY's 1994 ($277), 1996 ($3,488) and 1997 ($126,312). Further refunds of remaining pre-1998 balances will not be made until all pending appeals from this period are resolved, but $130,077 must be kept in reserve for potential refunds until these appeals are resolved or refunds are made.

FDA's FY 1998 collections currently exceed the appropriations limit by $727,016. Some FY 1998 requests for refunds or waivers are still pending, however. If the net collections still exceed the appropriation limit after these waiver requests are settled, then FDA will set fees at a lower level in the future to offset these surplus collections. Therefore, this $727,016 must be kept in reserve as an offset for future collections until these requests are settled.

RESERVE FOR FUTURE OPERATIONS

The table below provides a summary of carryover balances as of September 30, 2003, and anticipated claims on those balances. Included in those claims is also a requirement, from the congressional action on the agency's FY 2004 appropriation, to spend $3.6 million of the carryover funds to support a move of CDER drug review staff into the new White Oak facility in FY 2004.

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 at least 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 2004 operations for approximately 1.4 months.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CARRYOVER BALANCE
As of September 30, 2003

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 2004	$3,625,000
Available for Allocation	$27,713,683
TOTAL Carryover Balance	$32,195,776

SUMMARY OF RECEIVABLES AND PAYMENTS DEFERRED AND REFUNDS OF FEES PAID BUT PENDING WAIVER RESOLUTION

At the end of FY 2003, in addition to the cash collected, FDA had receivables totaling $6,628,759. An allowance for loss on accounts receivable has been recorded at $670,473, which consists of $120,366 of accounts receivable greater than one year in arrears, and $550,107 that is deferred and will not be payable until a final decision is made on pending waiver requests.

Waivers or exemptions that will be granted will have to be met from cash realized as accounts receivable materialize or from available carryover balances. Given past experience, amounts received from accounts receivable balances and available carryover balances should adequately cover the cost of such waivers and exemptions.

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 2002 and FY 2003 by organization 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. 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, 2002 and 2003

FDA Component	FY 2002	FY 2003
Center for Drug Evaluation and Research (CDER)	$209,823,215	$250,370,170
Center for Biologics Evaluation and Research (CBER)	$90,039,433	$110,132,866
Field Inspection and Investigation Costs (ORA)	$19,200,869	$19,098,382
Agency General and Administrative Costs (OC)	$28,563,982	$29,840,492
Total Process Costs	**$347,627,499**	**$409,441,910**
Amount from Appropriations	$185,815,399	$209,287,410
Amount from Fees	$161,812,100	$200,154,500

The costs for all components except Field Inspection and Investigation rose in FY 2003. This increase primarily reflects additional personnel hired by CDER and CBER in FY 2003 and mandatory increases in pay rates for Federal employees. The decrease in field inspection and investigation costs is due to the recent decrease in the number of applications submitted, and increased reliance on recently completed inspection reports, if they are satisfactory, instead of automatic new pre-approval inspections.

The Agency General and Administrative Costs, though up slightly from FY 2002 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 2003.

MANAGEMENT CHALLENGES FOR FY 2004

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 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 2004 Performance Plan assumes increased efficiencies through administrative and information technology 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 for information technology consolidation and administrative consolidation, managing the PDUFA program without compromising staffing and performance levels will be a sizable challenge.

The second major resource challenge relates to user fee funding. Under the provisions of PDUFA, funds from user fees are to increase from $222.9 million in FY 2003 to well over $240 million in FY 2004. However, under a series of continuing resolutions, FDA had to keep its user fee spending for FY 2004 at the previous year's levels for the first 4 months of FY 2004. This limitation in the availability of user fee resources for the first one-third of FY 2004, and lower than requested final appropriations, have challenged the drug review program.

In FY 2004, a key PDUFA IT investment is the development of a common electronic submission solution for CBER and CDER. This includes the establishment of a cross Agency team to develop a target electronic submission architecture. A cross-Center group has been established to pilot a common portal for electronic submissions. In addition, the integration of the CBER and CDER systems will be a major activity due to the biologic therapeutic product transfer effective October 1, 2003. As part of the integration an analysis will be done to determine the feasibility of consolidating tracking and document management systems to meet the business needs of both CBER and CDER.

In FY 2004, FDA will also continue the implementation of the new provisions of PDUFA III that permit using fee revenue to support certain risk management activities. This represents a change in how these revenues may be used, and an opportunity for the agency to enhance patient safety and work proactively to manage risks and reduce preventable adverse events.

FDA will continue to be challenged by the need to hire, train, and retain qualified reviewers in FY 2004. FDA's experienced reviewers are in demand and 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. Continuing to recruit and retain top rate professional staff is among the Commissioner's highest priorities.

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 they were met was provided earlier on page 2. A description of each of these conditions is provided below, with an explanation of how the condition was met in FY 2003.

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 2002, the fiscal year preceding FY 2003, is 179.8. The consumer price index for April 1997 is 160.2. The result of this dividing 179.8 by 160.2 is an adjustment factor of **1.1223** for FY 2003.

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) times the adjustment factor. FDA's total FY 1997 Salaries and Expenses appropriation, excluding fees, was $819,971,000. Multiplying this amount by the adjustment factor of 1.1223 results in an adjusted FY 1997 Salaries and Expenses Appropriation, excluding fees, of $920,253,453.

For FY 2003, 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 $1,268,098,000. Since the FY 2003 appropriation amount exceeds the FY 1997 adjusted amount, the first condition was met.

The **second condition** comes from Section 736(g)(2)(A)(i). It states 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 specifying amounts collectable from fees during FY 2003 on February 20, 2003 (Public Law 108-7). It provided $222,900,000 to come from PDUFA fees. Thus, the second condition was met.

The **third condition** in the Act, 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 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 1.1223, FDA's 1997 adjusted minimum spending for the process for the review of human drug applications from appropriations, exclusive of fees, must be $166,055,159 in FY 2003.

The FDA costs (obligations) from appropriations for the process for the review of human drug applications for FY 2003 was $209,287,410. Since this is greater than the adjusted FY 1997 amount ($166,055,159) the third condition was met.

The table below shows amounts FDA spent on the process for the review of human drug applications in FY 2002 and 2003 and also shows the adjusted FY 1997 amount that had to be spent from appropriations. It also shows the amount of these costs that was charged to appropriations and the amount met from user fee revenues each year.

FOOD AND DRUG ADMINISTRATION
OBLIGATIONS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2002 and September 30, 2003

	FY 1997 Adjusted for FY 2003	FY 2002	FY 2003
From Appropriations	$166,055,159	$185,815,399	$209,287,410
From User Fee Revenues		$161,812,100	$200,154,500
Total Obligations		$347,627,499	$409,441,910

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, 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 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 FY's 1999, 2000, 2001, 2002, and 2003, and pending waiver requests for fees payable from the same periods.

EXEMPTIONS AND WAIVERS AS OF SEPTEMBER 30, 2003

Does not Include Data on FY 2004 Waivers Pending or Granted in FY 2003

Exempted Application Fees 1

	FY 1999	FY 2000	FY 2001	FY 2002	FY 2003	
Orphan Product	14.5	16.3	14.5	10.0	13.5	
Pediatric Supplements	5.3	12.6	19.0	4.5		2
Previously Submitted				7.5	3.0	3
Total Exemptions	19.8	28.9	33.5	22.0	16.5	
TOTAL -Exemptions Granted	**$5,377,570**	**$8,250,743**	**$10,373,175**	**$6,893,040**	**$8,801,100**	

Waivers Granted

APPLICATIONS 1						
Small Business Waivers	7.0	8.3	12.0	6.0	14.3	4
Miscellaneous Waivers	4.5	8.3	10.3	1.0	7.0	5
Value of Waivers Approved	$3,131,243	$4,714,710	$6,889,646	$2,193,240	$11,334,750	
PRODUCTS:						
Waivers Approved	24.0	19.0	17.9	10.0	30.9	
Value of Waivers Approved	$440,736	$379,221	$391,867	$216,300	$1,001,160	
ESTABLISHMENTS:						
Waivers Approved	12.5	11.5	10.4	7.3	16.5	
Value of Waivers Approved	$1,604,795	$1,636,926	$1,516,242	$1,028,876	$3,463,350	
TOTAL--Waivers Granted	**$5,176,774**	**$6,730,857**	**$8,797,754**	**$3,438,416**	**$15,799,260**	

Waivers Pending Decisions

	FY 1993-1999	FY 2000	FY 2001	FY 2002	FY 2003
APPLICATIONS:					
Waivers Pending	1		0		6
Allowance for Pending Waivers	$272,282	$0	$0		$3,200,400
PRODUCTS:					
Waivers Pending	6.0	2.0	3.0	8.3	22.0
Allowance for Pending Waivers	$68,373	$39,918	$65,676	$179,529	$712,800
ESTABLISHMENTS:					
Waivers Pending	2.0	0.5	1.5	4.5	8.8
Allowance for Pending Waivers	$463,153	$70,986	$218,984	$630,491	$1,853,417
TOTAL--Waivers Pending	**$803,808**	**$110,904**	**$284,660**	**$810,020**	**$5,766,617**

Total Pending for all years: $7,776,008

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 (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 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 2003 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 Management, and the Office of Communications,

Training, and Manufacturers Assistance. The 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.

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 2003

The time reporting systems operated by CBER and CDER indicated the 66 percent of all time spent in CBER and 75 percent of all time spent in CDER in FY 2003 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 2002 and 2003.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
As of September 30, 2002 and 2003

Cost Component	FY 2002	FY 2003
Staff Years Utilized	153	147
ORA Average Salary & Benefits	$77,987	$79,696
Salary and Benefits	$11,931,986	$11,715,260
Operations and Rent	$7,268,883	$7,383,122
Total	**$19,200,869**	**$19,098,382**

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. The reduction in ORA staff-years dedicated to the review of human drug applications is a result of two factors. First, ORA increasingly is relying on the latest data in its files, if an inspection has been completed recently, rather than initiating a new inspection prior to a drug approval. Second, the relatively low number of new drug and biologic applications in FY 2003 resulted in fewer assignments to the field for pre-approval inspections.

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 2003, OC was comprised of the following offices:

- Immediate Office of the Commissioner
- Office of the Chief Counsel

- Office of Equal Opportunity
- Office of the Administrative Law Judge
- Office of Communication and Constituent Relations
- Office of Science Coordination and Communication
- Office of International Affairs
- Office of Policy, Planning and Legislation
- 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, $28,563,982 and $29,840,492 in general and administrative obligations were dedicated to the human drug review process in FY's 2002 and 2003, respectively. These are total costs, including funds obligated both from appropriations and from fees. The Agency general and administrative obligations in FY 2003 accounted for about 7.3 percent of the total FY 2003 cost of the process for the review of human drug applications. This is down from 8.2 percent in FY 2002, and is down substantially from the 10.4 percent in FY 1998 at the beginning of PDUFA II. This means that the percent of process costs devoted to overhead has been reduced by 30 percent since 1998. This remarkable sustained reduction in overhead is the result of FDA's commitment to increase efficiency in its operations.