FY 1998 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

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) 1998.

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. Overall FDA appropriations, excluding fees, must exceed FDA's overall FY 1997 appropriation (excluding fees and adjusted for inflation).
2. Fee revenues collected must be specified in FDA's appropriations.
3. FDA must spend on the drug review process at least as much from appropriated funds as it spent in FY 1997, adjusted for inflation.

This report describes how those specific statutory conditions or "triggers" were met in FY 1998. The statements and tables included in this report also provide information on the user fee revenues and expenditures in FY 1998, and on the carryover balance. Comparative data for earlier periods is also provided.

In FY 1998, FDA collected $132.7 million in user fees and had estimated receivables of $13.8 million. The $132.7 million collected includes $113.1 million in FY 1998 fees and $19.6 million in fees from previous years. Most of the latter are second-half application fees from submissions prior to October 1, 1997, when the second half of the application fee was not due until FDA completed action on the application. Under FDAMA amendments, the full application fee is due upon submission for all applications received on or after October 1, 1997. The result was a one-time spike in fee revenues in FY 1998. In FY 1999 FDA expects to receive a few more second-half fees, but a far smaller number.

In FY 1998, FDA spent $101.6 million from PDUFA revenues. The FY 1998 expenditures were significantly constrained because of concerns that arose about a potential shortfall in fee revenues in FY 1999. As a result, many acquisitions were delayed and many hiring actions were deferred in order to preserve funds for use in FY 1999.

Over 70 percent of the FY 1998 expenditures went for employee pay and benefits. Throughout FY 1998, user fees financed 708 more staff-years for the drug review process than were utilized in 1992 (before PDUFA was enacted). This large 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 1998 went for 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).

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BACKGROUND

PDUFA authorized FDA to collect fees from the pharmaceutical industry to augment FDA's base resources for a 5-year period. These additional resources were 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 was very successful and, with support from the pharmaceutical industry and the Administration, Congress amended and extended it through FY 2002 by enacting the FDAMA.

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 1998 PDUFA Performance Report, which discusses FDA's progress in meeting the goals referred to in FDAMA, was released in December 1998. This is FDA's FY 1998 PDUFA Financial Report, covering the period October 1, 1997, through September 30, 1998.

As required by statute, this report presents the legal requirements 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 1998. This report also presents 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 Officer's 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 1997. The OIG rendered a qualified opinion on FDA's financial statements for FY 1997. The qualifications expressed related to accounting for property (a minor part of PDUFA resources) and accounting for grants (which do not involve PDUFA funds). The OIG audit report on FDA's FY 1998 financial statement is expected to be available later in FY 1999. FDA expects the FY 1998 audit report to reflect substantial improvement since FY 1997.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 1998

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 1998 are presented in more detail in Appendix A. FDA did meet all necessary conditions in FY 1998, as summarized below.

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 1998, FDA's Salaries and Expenses Appropriation (excluding user fees) totaled $857,501,000. FDA's FY 1997 Salaries and Expenses Appropriation (excluding user fees, and adjusted for inflation as specified by statute) was $819,971,000. Therefore, since the FY 1998 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 FDA's appropriations. For FY 1998 FDA's appropriation acts specified that $117,122,000 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 drug review process. The specified minimum is the amount FDA spent on the drug review process 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 1998 the adjustment factor is one. As this report shows, in FY 1998 FDA used $151,836,635 from appropriated funds for the drug review process, which exceeds the specified minimum amount. Thus, the third condition has been met.

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

USER FEE REVENUES

The PDUFA specified the user fee revenues to be collected from product, establishment, and application fees. Only half of the application fee was due upon submission of an application for FY 1993 through FY 1997. The remainder of the application fee is due 30 days from the date FDA issues an invoice after issuance of an action letter related to the application. Thus, fee revenue related to submissions received in those fiscal years may come due and be collected in succeeding years. Under FDAMA the full application fee is due upon submission of an application for applications submitted on or after October 1, 1997, eliminating the need to invoice when an action letter is issued.

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 will be dealt with in the section of carryover balances on page 7. 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, 1998

	FY 1997	FY 1998
Fees Collected:		
Product Fees	$29,911,200	$38,055,777
Establishment Fees	$29,040,690	$43,224,464
Application Fees	$31,824,836	$31,777,616
TOTAL FEES COLLECTED:	$90,776,726	$113,057,857
Fees Receivable:		
Product Fees	$105,600	$3,755,382
Establishment Fees	$2,198,300	$2,910,303
Application Fees	$1,178,750	$128,423
TOTAL FEES RECEIVABLE:	$3,482,650	$6,794,108
Total User Fee Revenues:	$94,259,376	$119,851,965
Additional Unbilled Fees	$2,613,750	-
TOTAL PROJECTED REVENUES:	$96,873,126	$119,851,965

The Fees Receivable for FY 1997 of $3,482,650 includes $2,508,900 of deferred collections, pending final resolution of waiver requests. Whether these actually result in collections depends on the outcome of these pending waiver requests. The remainder is primarily the second half of FY 1997 application fees that were billed late in FY 1998. The Fees Receivable for FY 1998 of $6,794,108 includes $1,029,258 of deferred collections, pending final resolution of waiver requests. Most of

the balance from FY 1998 is product and establishment fees billed near the end of the fiscal year.

Additional Unbilled Fees of $2,613,750 for FY 1997 submissions were not billed or billable as of September 30, 1998, and have not been included in total receivables for FY 1997. These represent second-half application fees to be billed and collected upon completion of the first review action on applications filed in FY 1997. Therefore, the total projected revenues, before estimated waivers and reductions, related to FY 1997 submissions are $96,873,126 (94,259,376 + $2,613,750), and total estimated revenues related to FY 1998 submissions are $119,851,965.

A summary of exemption and waiver actions for FY's 1993 through 1996, FY 1997, and FY 1998 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 1998, FDA continued to improve and expedite the activities involved with the process for review of human drug applications, obligating $101,615,000 of the user fees collected.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
as of September 30, 1998

Expense Category	FY 1997	FY 1998
Personnel Compensation and Benefits	$62,039,000	$71,186,000
Travel and Transportation	$2,270,000	$2,813,000
Communications	$1,183,000	$1,196,000
Contract Services	$13,637,000	$18,084,000
Equipment and Supplies	$5,094,000	$8,215,000
Other	$66,046	$121,000
TOTAL OBLIGATIONS:	$84,289,046	$101,615,000

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. 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 708 more FTE in FY 1998 for PDUFA activities than were utilized in FY 1992. This is an increase of 12 over the 696 additional FTE fees supported in FY 1997. FDA's payroll costs paid from user fee funds in FY 1998 totaled $71,186,000—over 70% of the funds expended. This includes all pay and benefits for the additional 708 FTE and costs of the FY 1998 payroll increases for the baseline FTE.

A substantial amount of the remaining funds were spent on information technology. FDA has begun an Agency-wide information technology (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 PDUFA. 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 1998, several technical standards have 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 $101,615,000, while larger than FY 1997 amounts, represents a 10 percent reduction below the planned expenditure level. This was a result of deliberate actions taken in the last few months of the fiscal year. In FY 1998 FDA realized that the number of fee-paying applications would be substantially less than the 152 originally projected—closer to 120. This was the first time in six years that receipts fell below the forecast. The shortfall was the compound result of both (1) fewer drug and biologic applications submitted by industry than in the previous year and (2) a larger than expected increase in the number of submissions exempt from fees under new FDAMA provisions.

The real significance of this shortfall would be felt in FY 1999 revenues, because under FDAMA amendments the number of fee-paying applications became a pivotal factor in total fee revenue for the next year. Early estimates of FY 1999 revenues ran 30 percent below plans, and sharply below FY 1998 levels, while PDUFA workload (including investigational new drug submissions and manufacturing supplements that are not counted in fee-paying submissions) increased.

Due to the anticipated shortfall in revenue, FDA felt it prudent to curtail the hiring of personnel and defer expenditures in the last few months of the fiscal year. The result of these savings in FY 1998 enables FDA to carry forward funds for use in FY 1999.

CARRYOVER BALANCES

Under PDUFA and FDAMA, any fees collected and not spent 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 1998 increased the carryover balance by $31,056,143. This large increase is the combined result of:

- the one-time spike in FY 1998 collections, attributable to collection of both (1) the second-half of application fees for many prior fiscal year submissions, (2) full application fees for all FY 1998 submissions; and
- actions previously mentioned to constrain FY 1998 obligations in order to conserve funds for use in FY 1999.

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, 1998

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			

The balances above do not include estimated receivables from FY 1998 and prior years, which total $13,759,458. It is important to note that while the carryover balance grew substantially in FY 1998, there are also a number of claims on these funds. Those claims (refunds, reserve for future operations, and FY 1999 operating needs) are explained below. As a result of these claims, we expect a substantial reduction in the carryover balance at the end of FY 1999.

COLLECTION CEILINGS AND POTENTIAL REFUNDS

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 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 refunded.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF FEES COLLECTED, COLLECTION CEILINGS, AND POTENTIAL REFUNDS
as of September 30, 1998

Fiscal Year	Collections Realized	Collection Ceiling	Potential Refund
1993	$35,949,490	$36,000,000	-
1994	$56,556,650	$56,284,000	$272,650
1995	$77,765,800	$79,423,000	-
1996	$87,332,885	$84,723,000	$2,609,885
1997	$90,776,726	$87,528,000	$3,248,726
1998	$113,057,857	$117,122,000	-
		Total:	$6,131,261

As of September 30, 1998, collections have exceeded appropriations in FY's 1994 ($272,650), 1996 ($2,609,885) and 1997 ($3,248,726). A total of $6,131,261 will have to be refunded, decreasing the carryover balance. The amounts to be refunded for FY's 1996 and 1997 are likely to increase because more second-half application fees will be paid for these years. 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. Resolving these waivers and refunds, particularly for years in which refunds are due, is a priority in FY 1999.

When the refunds are made, it is FDA's intention to pro-rate the amount based on the total fees paid (application, establishment, and product fees combined) by each firm for the specific fiscal year.

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 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 1999 the Agency needs to carry forward $39.5 million to cover essential future operating costs.

AMOUNT ALLOCATED IN FY 1999

In addition to the items discussed above, $25 million from carryover balances has been allocated to FDA

components in FY 1999. Acquisitions and hiring were postponed in FY 1998 in order to have this amount available for essential operations and personnel in FY 1999. The availability of these funds assures that performance goals for FY 1999 will be met.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CLAIMS ON CARRYOVER BALANCE
as of September 30, 1998

Nature of Claim	Amount
Reserve for Refunds	$6,131,261
Reserve for Future Operations	$39,477,000
Amount Allocated in FY 1999	$25,000,000
TOTAL CLAIMS	$70,608,261

The chart above summarizes all the claims on the carryover balance. The total exceeds the available carryover balance by $3.1 million because it takes into consideration the anticipated collection of receivables.

SUMMARY OF RECEIVABLES AND PENDING WAIVER REQUESTS

At the end of FY 1998, in addition to the cash collected, FDA had receivables totaling $13,759,458. As shown in Appendix B, there were waiver requests totaling $7,020,858 pending at the end of FY 1998. A reserve in this amount has been established within accounts receivable. The balance, exclusive of this reserve, is $6,738,600. Over half of that amount will be used to satisfy the claims on the carryover balance described above.

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 1997. 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 1997 and 1998 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, 1998

FDA Component	FY 1997	FY 1998
Center for Drug Evaluation and Research (CDER)	$127,686,288	$144,227,003
Center for Biologics Evaluation and Research (CBER)	$66,102,113	$66,275,840
Field Inspection and Investigational Costs (ORA)	$14,849,704	$16,904,301
Agency General and Administrative Costs	$23,610,630	$26,044,491
Total Process Costs	**$232,248,735**	**$253,451,635**
Amount from Appropriations	$147,959,689	$151,836,635
Amount from Fees	$84,289,046	$101,615,000

The costs for CDER rose significantly in FY 1998. This reflects increased staffing levels and information technology expenditures as CDER gears up for the new challenges imposed by PDUFA goals for FY's 1998-2002. CBER expenditures remained relatively flat, in spite of substantial increases in pay costs in FY 1998, because research resources that had been allocated to CBER from PDUFA revenues are being phased out. Much of the additional review staff that CBER will need to meet new goals will be provided by reassignment of research staff to review work.

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

MANAGEMENT CHALLENGES FOR FY 1999

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 1999, FDA will be challenged to sustain these improvements, meet increasingly difficult performance goals, and position the agency to meet future goals.

One of the changes to PDUFA included in FDAMA amendments was the incorporation of a workload adjuster. Its purpose was to assure that fee revenues would increase proportionally when workload increases, providing additional revenues to help the agency respond. Likewise, when workload decreased, revenues were to decrease. FDAMA made the number of fee-paying applications the surrogate for PDUFA workload. With the benefit of hindsight, we now realize that a single factor (the number of fee-paying applications) is not the best surrogate for PDUFA workload, which is really an aggregate of many complex components.

In FY 1998, the number of applications submitted to FDA for review declined for the first time in 6 years, as noted in the FY 1998 PDUFA Performance Report released in December. FDAMA amendments exacerbated this decline, causing over 30 more of these applications to be exempt from fees than would have been exempt previously. More details on these increased exemptions can be found in Appendix B. Total PDUFA workload, however, which includes this increasing volume of items exempt from fees as well as an increasing volume of work not subject to fees (investigational new drug submissions and manufacturing supplements) increased in FY 1998. As a result the new workload adjuster does not reflect real changes in PDUFA workload. A major challenge for FY 1999 will be addressing longer-term actions that may be necessary to remedy problems with the workload adjuster.

In FY 1999 FDA will continue working toward the goal of receiving applications electronically by the end of FY 2002. This represents a major change in how FDA does business and 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 1999 FDA will continue to be challenged by the need to hire, equip, and train qualified reviewers. FDA's skilled, experienced reviewers are in demand and have excellent employment opportunities. The Agency experienced attrition of about 10 per cent of its review staff in FY 1998. Recruiting and training new staff is a constant challenge.

Finally, the Agency is challenged 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 1998.

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 an adjustment 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 1997 (160.2) divided by the consumer price index of April of the fiscal year immediately preceding FY 1998 (which is also April 1997). The result of this division is a factor of one. The second calculated factor, 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), divided by the domestic discretionary budget authority for the fiscal year immediately preceding FY 1998. Since this is the same number, this factor is also one. Since these two numbers both equal one, the lower of these two numbers is also one. Accordingly, the adjustment factor for FY 1998 is one.

FDA's total FY 1997 Salaries and Expenses appropriation, excluding fees, was $819,971,000. For FY 1998, FDA's total Salaries and Expenses appropriation, excluding user fees, was $857,501,000. Since the FY 1998 amount exceeds the FY 1997 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 first appropriation act (Public Law 105-86) specifying amounts collectable from fees during FY 1998 was signed by the President on November 18, 1997. It provided $91,204,000 to come from fees collected. A supplemental appropriation (Public Law 105-174) signed by the President on May 1, 1998 provided an additional $25,918,000 that was to come from fees collected. Combining these two amounts, a total of $117,122,000 was provided in appropriation acts to come from user fees. 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. Applying the adjustment factor of one derived above,
FDA's 1997 adjusted costs for the process for the review of human drug applications is $147,959,689.

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

	Adjusted FY 1997	FY 1998
From Appropriations	$147,959,689	$151,836,635
From User Fee Revenues	$84,289,046	$101,615,000
Total Obligations	$232,248,735	$253,451,635

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 by well over 30. And this occurred in a year when the total number of applications (non-fee-paying and fee-paying) dropped for the first time in six years as well.

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.

The tables on the following page summarize the exemption and waiver actions taken by FDA for FY's 1993 through 1996, FY 1997, and FY 1998, and pending waiver requests from the same periods.

EXEMPTIONS AND WAIVERS

(Exemptions counted in Full Application Equivalents)

	FY 1993 Through FY 1996	FY 1997	FY 1998
Exemptions			
APPLICATIONS			
Exemptions Provided			
Orphan Product	Treated as Waivers	Treated as Waivers	16
Pediatric Supplements	Treated as Waivers	Treated as Waivers	8
Small Business	13	4.5	15
Total Exemptions	13	4.5	42
TOTAL VALUE OF APPLICATION EXEMPTIONS	**$2,349,000**	**$923,000**	**$10,659,109**
Approved Waivers			
APPLICATIONS			
Waivers Approved	56	9	2
Value of Waivers Approved	$8,249,750	$1,486,250	$513,702
PRODUCTS:			
Waivers Approved	141	40	18
Value of Waivers Approved	$1,477,000	$528,000	$334,638
ESTABLISHMENTS:			
Waivers Approved	33	11	10
Value of Waivers Approved	$3,623,000	$1,272,700	$1,161,707
TOTAL VALUE OF WAIVERS APPROVED:	**$13,349,750**	**$3,286,950**	**$2,010,047**
Pending Waivers			
APPLICATIONS:			
Waivers Pending	2	2	0
Allowance for Pending Waivers	$50,000	$205,000	$0
PRODUCTS:			
Waivers Pending	39	8	21
Allowance for Pending Waivers	$437,600	$105,600	$390,411
ESTABLISHMENTS:			
Waivers Pending	25	19	4.5
Allowance for Pending Waivers	$2,995,100	$2,198,300	$638,847
TOTAL ALLOWANCE FOR PENDING WAIVERS:	**$3,482,700**	**$2,508,900**	**$1,029,258**

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") define 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 which 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, 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

Since these inclusions and exclusions required accounting for of a newly-created subset of FDA activities, 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. Arthur Andersen & Company independently reviewed FDA procedures in 1995, and found the methodologies to be 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 of divisions and center-wide expenses are discussed below.

Review and Laboratory Components:

The review and laboratory components, as organized during FY 1998, 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 Drug Evaluation I	Office of Vaccines
Neuropharamacological Drug Products	Office of Therapeutics
Oncologic Drug Products	Office of Blood
Cardio-Renal Drug Products	Office of Establishment Licensing and Product Surveillance
Office of Drug Evaluation II	Allergenic Products and Parasitology
Metabolic and Endocrine Drug Products	Bacterial Products
Pulmonary Drug Products	Viral Products
Reproductive and Urologic Drug Products	Vaccines and Related Product Applications
Office of Drug Evaluation III	Cytokine Biology
Gastro-Intestinal and Coagulation Drug Products	Cellular and Gene Therapies
Anesthetic, Critical Care and Addiction Drug Products	Hematologic Products
Medical Imaging and Radiopharmaceutical Drug Products	Clinical Trial Design and Analysis
Office of Drug Evaluation IV	Application Review and Policy
Anti-Viral Drug Products	Transfusion Transmitted Diseases
Anti-Infective Drug Products	Hematology
Special Pathogens and Immunodulatory Drug Products	Blood Applications
Office of Drug Evaluation V	Establishment Licensing
Anti-Inflammatory, Analgesic, and Ophthalmologic Drug	Biostatistics and Epidemiology
Dermatologic and Dental Drug Products	Product and Quality Control
Over-the-Counter Drug Products	Monoclonal Antibodies
Office of Epidemiology and Biostatistics	Veterinary Services
Quantitative Methods and Research Staff	
Biometrics I, II, III, and IV	
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, and the Office of Compliance. In CBER, these components include portions of the Office of the Center Director, Office of Management, Office of Compliance, 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 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. Examples of the user fee excluded divisions include 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 69 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 not 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.

Types of Research

User fee related research is categorized based on its impact on the drug approval process:

Review of the Manufacturing Process

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

All 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 accumulates 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 1997 and 1998, respectively.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
as of September 30, 1998

Cost Component	FY 1997	FY 1998
Staff Years Utilized	171	180
ORA Average Salary	$60,585	$64,680
Salary and Benefits	$10,360,041	$11,642,314
Operations and Rent	$4,489,663	$5,261,987
Total	$14,849,704	$16,904,301

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 Policy
- Office of External Affairs
- 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 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, $23,610,630 and $26,044,491 in General and Administrative obligations were dedicated to the human drug review process in FY's 1997 and 1998, respectively. Although the costs applicable to the process have increased in FY 1998 (due to the increase in federal salary costs) the Agency General and Administrative costs account for only 10.4 percent of the total FY 1998 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.