FY 2002 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

MARCH 2003

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

March 27, 2003

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 (section 104(b) of the Food and Drug Administration Modernization Act of 1997 (FDAMA)). This report covers fiscal year (FY) 2002, 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 2002, comparative data for earlier periods, and details the amounts carried over at the end of each year that remain available. For FY 2002, FDA collected $143 million in user fees, and spent $162 million. The spending included balances collected in earlier periods that remained available. Almost 70 percent of the fees 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.

We are pleased that Congress enacted the reauthorization of PDUFA (PDUFA III) through FY 2007 last June, well in advance of the expiration of PDUFA II. Beginning in FY 2003, PDUFA III authorizes higher levels of fee revenue to support the drug approval process.

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 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 reauthorized by the Food and Drug Administration Modernization Act of 1997 (FDAMA or PDUFA II). This report covers fiscal year (FY) 2002.

The PDUFA II specifies that the following three conditions must be satisfied each year in order for FDA to collect and spend PDUFA fees:

1. FDA's overall salaries and expenses appropriation, excluding fees, must exceed FDA's overall FY 1997 salaries and expenses appropriation (excluding fees and adjusted for inflation).
2. Fee revenues collected must be specified in Appropriation Acts.
3. FDA must spend at least as much from appropriated funds for the review of human drug applications as it spent in FY 1997, adjusted for inflation.

This report describes how those specific statutory conditions or "triggers" were met in FY 2002. The statements and tables included in this report also provide information on the user fee revenues and expenditures in FY 2002, and on the carryover balance. Comparative data for earlier periods are also provided.

For FY 2002, FDA collected $143.3 million in fees and, at the end of the year, FDA also had receivables of $1.8 million.

In FY 2002, FDA spent $161.8 million from PDUFA revenues—$18.5 million more than its net collections for the year. This resulted from planned spending of carryover balances in order to fund staffing levels to permit FDA to meet increasingly challenging PDUFA goals that involve a wide range of activities, not just review of the types of applications for which fees were paid.

A drop in fee-paying applications in FY 2001 caused the projected level of fees to be collected for FY 2002 to drop by about $22 million below earlier projections. This drop in revenue is not an indication that the overall FDA review workload has declined—only that a large and increasing number of industry submissions were in categories for which fees were not paid. However, the drop in projected revenues forced FDA to constrain expenditures in FY 2002 in order to assure that funds would be sufficient to pay employees working in the drug review process.

Recognizing the necessity of reauthorizing PDUFA before the end of FY 2002 to assure continuity of operations, Congress enacted the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which includes the Prescription Drug User Fee Amendments of 2002 (PDUFA III) reauthorizing user fees through FY 2007. The President signed PDUFA III into law on June 12, 2002. Challenges facing FDA in FY 2003 include hiring and training additional staff to meet the PDUFA III goals. Until the FY 2003 appropriation was enacted, however, spending under terms of a series of continuing resolutions delayed the hiring of additional staff.

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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 and the Administration, Congress amended and extended it through FY 2002 (PDUFA II).

Under PDUFA II an application fee must be submitted when certain new drug applications (NDA's) or biologic license applications (BLA's) 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. PDUFA II authorizes FDA to set 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 II 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 2002 PDUFA Performance Report, which discusses FDA's progress in meeting the goals referred to in PDUFA II, is being separately transmitted to Congress. This is FDA's FY 2002 PDUFA Financial Report, covering the period October 1, 2001 through September 30, 2002.

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 2002. This report also presents FY 2002 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 II, 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 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 2002. This is the most favorable category of audit opinion.

MEETING THE LEGAL CONDITIONS FOR USER FEES IN FY 2002

PDUFA II 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 2002 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 2002, 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 $1,083,854,000. FDA's FY 1997 total Salaries and Expenses appropriation, excluding user fees, and adjusted as required by the statute, was $905,411,978. Therefore, since the FY 2002 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 2002, FDA's Appropriation Act specified that $161,716,000 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 $163,377,089. In FY 2002, FDA obligated $185,815,399 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 II specifies that fee revenues are to be collected from establishment, product, and application fees. The statute specifies annual application fee amounts and how they are adjusted each year for inflation. Fees for establishments and products are set each year so that the total amount of revenue collected from each category (establishment fees and product fees) equals the revenue FDA expects to collect from application fees that year.

Under PDUFA II, 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 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, 2002

	FY 2001	FY 2002
Fees Collected:		
Product Fees	$51,666,580	$49,802,492
Establishment Fees	$53,596,320	$51,872,176
Application Fees	$33,204,819	$41,656,543
TOTAL FEES COLLECTED:	**$138,467,719**	**$143,331,211**
Fees Receivable:		
Product Fees	$131,352	$1,059,825
Establishment Fees	$0	$714,200
Application Fees	$158,496	$0
TOTAL FEES RECEIVABLE:	**$289,848**	**$1,774,025**
Total User Fee Revenues:	**$138,757,567**	**$145,105,236**

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 2001, even if it is received in FY 2002, is attributed to FY 2001 revenues. Totals reported for each year are net of any refunds for that year.

The Fees Receivable for FY 2001 of $289,848 include deferred collections of $116,779, pending final resolution of waiver requests. Most of the FY 2002 accounts receivable are product and establishment fees billed near the end of the fiscal year. Fees receivable for FY 2002 also include deferred collections of $253,424 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 II. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C. In FY 2002, FDA obligated $161,812,100 from user fee revenues.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF USER FEE OBLIGATIONS BY EXPENSE CATEGORY
as of September 30, 2001 and 2002

Expense Category	FY 2001	FY 2002
Personnel Compensation and Benefits	$107,331,472	$112,852,095
Travel and Transportation	$3,757,259	$3,834,105
Rent	$5,860,000	$1,040,000
Communications	$628,269	$1,288,359
Contract Services	$31,246,400	$31,834,035
Equipment and Supplies	$11,614,462	$10,539,764
Other	$275,138	$423,742
TOTAL OBLIGATIONS	$160,713,000	$161,812,100

FDA dedicated 1,277 FTE's (Full Time Equivalents or 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 FTE 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 2002, PDUFA fees and appropriations paid for 1,060 more FTE's 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 2002 represented over 70 percent of the funds expended. This includes all pay and benefits for the additional FTE's and costs of the FY 2002 payroll increases for all drug review process FTE's.

A substantial amount of the remaining funds were spent on information technology (IT). FDA is engaged in an Agency-wide IT program to support the transition from a largely paper-based regulatory submission and review environment to an electronic environment. This effort is called the Electronic Regulatory Submission and Review (ERSR) program. ERSR is comprised of a variety of projects, each of which is designed to satisfy a different part of the overall PDUFA IT goal that:

> The Agency shall develop and update its information management infrastructure to allow, by FY 2002, the paperless receipt and processing of investigational new drugs (IND's) and human drug applications, as defined in PDUFA, and related submissions.

The major ERSR project areas and FY 2002 activities are described below.

- **Standards and Guidance**. These projects promote consistent exchange of electronic information between the FDA and external constituents. In FY 2002, FDA continued participation in the International Conference on Harmonization (ICH) expert working groups focusing on electronic standards for transmission of regulatory information. Development of the electronic common technical document for the technical content of sections relevant to the IND/NDA/BLA was initiated. Similar development was also started on general administrative information and labeling. The FDA participated in international standards development organizations working on data standards for clinical study data.
- **Capability to Receive Electronic Submissions**. These projects implement procedures and technology to support electronic submissions in lieu of paper. In FY 2002, written guidance was provided for industry to follow in preparing various types of electronic submissions. Additional work was done toward improving the efficiency of electronic submissions for both industry and the agency by harmonizing the technology used for submission of human drug applications with the submission of exemptions for IND's and other related submissions. Industry training was provided at technical workshops and IT conferences hosted by third-party organizations. Working collaboratively with program staff, IT staff provided input and assistance for these activities.
- **Electronic Review**. These projects enable FDA reviewers and field inspectors to conduct review activities in an electronic environment. In FY 2002, electronic submissions that conform to the established standards and industry guidance were transmitted via acceptable media to FDA. In FY 2002, major enhancements were initiated to systems developed to provide an automated means for creating, managing, and archiving internally generated review documents. In addition, enhancements continued on systems that track the status and progress of submissions sent to FDA, generate mandatory user fee reports, and enable tracking of milestones and workload statistics for improved management and accountability.
- **Updated Infrastructure**. These projects include the implementation of underlying technologies required to support the transition to a paperless review environment. In FY 2002, FDA's PDUFA IT systems were supported by an infrastructure including standard hardware and software (i.e., desktops, networks, office automation tools, servers). FDA's standard desktop software suite for the reviewer community is in compliance with FDA's information systems architecture initiative. In addition, foundational support, such as training and technical support, was provided to the FDA review community.

The total expenditure of $161,812,100 in FY 2002 is an increase of less than 1 percent over FY 2001 amounts spent from fee revenue. This spending amount is about $25 million lower than the latest PDUFA II Five-Year Plan Update, but is still in excess of the revenues FDA collected in FY 2002. This change in the spending plan in FY 2002 was necessary because FDA collected less revenue than expected in FY 2001 due to a drop in application fee revenues causing PDUFA II formulas that projected revenue in FY 2002 to drop by an additional $22 million below earlier projections. In response to these financial realities, FDA constrained expenditures in FY 2002, in order to assure that funds would be available to continue to pay existing staff working on the drug review process for the entire year. The formulas that caused much of this reduction in fee revenues in FY 2002 have been amended in the PDUFA III reauthorization for the next 5 years that was signed by the President on June 12, 2002.

CARRYOVER BALANCES

Under PDUFA and PDUFA II 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 2002 decreased the carryover balances by $12,733,161.

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, 2002

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			

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 collections balance shown above for FY 2002 of $149,078,939 is substantially more than the FY 2002 collections balance on page 3 of $143,331,211. Most of this difference is the result of collections during FY 2002 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, collections in excess of amounts stated in appropriations 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, 2002

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	$117,756,061	$117,122,000		$634,061
1999	$125,501,406	$132,273,000		-
2000	$141,731,859	$145,434,000		-
2001	$138,467,719	$149,273,000		-
2002	$143,331,211	$161,716,000		-
		Total:	**$130,077**	**$634,061**

RESERVE FOR REFUNDS AND OFFSET FOR FUTURE COLLECTIONS

As of September 30, 2002, 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 $634,061. 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 $634,061 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, 2002. Due to a change in PDUFA III law requiring establishment and product fees to be paid for FY 2003 and future 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 2003 operations for approximately 1.2 months.

FOOD AND DRUG ADMINISTRATION
SUMMARY STATEMENT OF CARRYOVER BALANCE
as of September 30, 2002

Status of Carryover Funds	Amount
Reserve for Refunds of Excess Collections	$130,077
Reserve for Future Collection Offset	$634,061
Available for Allocation	$21,919,087
TOTAL Carryover Balance	$22,683,225

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

At the end of FY 2002, in addition to the cash collected, FDA had receivables totaling $2,863,469. An allowance for loss on accounts receivable has been recorded at $557,159, which consists of $120,366 of accounts receivable greater than one year in arrears, and $436,793 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's 2001 and 2002 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 COST
as of September 30, 2001 and 2002

FDA Component	FY 2001	FY 2002
Center for Drug Evaluation and Research (CDER)	$194,878,267	$209,823,215
Center for Biologics Evaluation and Research (CBER)	$80,505,442	$90,039,433
Field Inspection and Investigation Costs (ORA)	$22,247,719	$19,200,869
Agency General and Administrative Costs (OC)	$25,773,229	$28,563,982
Total Process Costs	**$323,404,657**	**$347,627,499**
Amount from Appropriations	$162,691,657	$185,815,399
Amount from Fees	$160,713,000	$161,812,100

The costs for all components except Field Inspection and Investigation rose slightly in FY 2002. This increase primarily reflects 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 2001 levels, have declined over the 5 years of PDUFA II as a percent of total spending on the drug review process. As reflected in Appendix D, the percent of drug review process costs devoted to agency general and administrative costs since 1998 has been reduced by 21 percent.

MANAGEMENT CHALLENGES FOR FY 2003

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.

The agency is gratified that Congress and the Administration have worked together with the agency and its stakeholders to achieve timely reauthorization of PDUFA for the next 5 years. On June 12, 2002, the President signed the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which includes the Prescription Drug User Fee Amendments of 2002 (PDUFA III) reauthorizing user fees and assuring the continuation and enhancement of the of prescription drug user fee program through FY 2007.

Under PDUFA III a number of changes were made to PDUFA II. A more stable fee structure and increased fee revenues should provide FDA with the resources needed both to continue to meet PDUFA II goals and to embark on several new PDUFA III initiatives aimed at further enhancing the drug review program.

The most significant tactical challenge facing FDA in FY 2003 is the need to hire additional staff for the drug review process, as authorized under PDUFA III. FDA must move quickly to hire additional staff now that FY 2003 appropriations which permit spending fee revenues at the higher levels authorized under PDUFA III have been enacted. The President signed the appropriation act permitting FDA to spend at the higher rates authorized under PDUFA III on February 20, 2003—almost 5 months into the fiscal year. As a result FDA will be able to utilize fewer additional staff years on the drug review process in FY 2003 than originally planned. This reduction in available human resources will challenge FDA in meeting performance goals for FY 2003.

In FY 2003, FDA will continue working toward the goal of receiving more applications, and more parts of applications, electronically. This major change in how FDA does business should provide significant savings to industry. Setting standards and sequencing the development and implementation of the necessary infrastructure to achieve this goal demands careful planning, constant monitoring, and vigilance with respect to newly emerging technologies.

After substantial deliberation, and in an effort to achieve a more efficient, effective, and consistent review program for human drugs and biologics, FDA has decided to move the review of therapeutic biologics from CBER into CDER. The employees to be transferred as a result of this reorganization represent about 31 percent of the CBER employees working on the process for the review of human drug applications, as defined in PDUFA. By organizing the drug development and review process around the disease being treated, informed by specific product and technology expertise, the Agency decision process for these products

can be made not only more consistent, but also more patient-centered and science-based. As anyone who has gone through organizational changes knows, the initial process creates understandable anxieties and uncertainties. In FY 2003 we will be challenged to prepare for the implementation of this reorganization, and actually begin the process, while maintaining and improving review quality, consistency and integrity. The Commissioner is committed to the enhanced review process that will result from this organizational change.

In FY 2003, FDA will also begin 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 2003. FDA's experienced reviewers are in demand and have excellent employment opportunities available to them. The agency experienced staff attrition of over 9 percent in FY 2002 in some major review disciplines in CDER (medical officers, consumer safety officers, and microbiologists). FDA has implemented a number of initiatives to reduce this attrition, including not only retention bonuses for reviewer mathematicians and statisticians but also efforts to facilitate review work from alternative work sites. Retaining review staff and recruiting and training new review staff is a constant challenge. Yet 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. Recruiting and retaining 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 more detailed presentation of each of these conditions is provided below, along with an explanation of how the condition was met in FY 2002.

For making the comparisons to determine if statutory conditions are met, 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 2001 (176.9), which is the fiscal year immediately preceding FY 2002, divided by the consumer price index for April 1997 (160.2). The result of this division is a factor of 1.1042.

The second calculated factor is the domestic discretionary budget authority for FY 2001 ($339.4 billion)[1], the fiscal year immediately preceding FY 2002, as it would have been reported in the final sequestration report submitted after the end of the 107th Congress, 2nd Session, divided by the domestic discretionary budget authority for FY 1997, as reported in the final sequestration report submitted after the end of the 105th Congress, 1st Session ($253.5 billion). The result of this division is a factor of 1.339.

[1] The amount of domestic discretionary budget authority for the previous year is no longer included in the final sequestration report, and has not been required by law since 1999. The figure used above ($339.4 billion for FY 2001) was provided by Office of Management and Budget staff in January 2003 as the amount that would have been included in the final sequestration report for non-defense discretionary spending had the requirement to report it still been in effect.

The lower of these two numbers is the first factor, 1.1042. Accordingly, the adjustment factor to be used for FY 2002 is **1.1042**.

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 1.1042 results in an adjusted FY 1997 Salaries and Expenses Appropriation, excluding fees, of $905,411,978.

For FY 2002, 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 $1,083,854,000. Since the FY 2002 appropriation amount exceeds the FY 1997 adjusted amount, the first condition was met.

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

The Appropriation Act (Public Law 107-76) specifying amounts collectable from fees during FY 2002 was signed by the President on November 28, 2001. It provided $161,716,000 to come from fees collected. Thus, the second condition was met, and fees may be collected.

The **third condition** in the Act, in Section 736(g)(2)(B), states:

> Fees shall only be collected and available to defray increases in the costs of the resources allocated for the process for the review of human drug applications (including increases in such costs for an additional number of full-time equivalent positions in the Department of Health and Human Services to be engaged in such process) over such costs, excluding costs paid from fees collected under this section, for fiscal year 1997 multiplied by the adjustment factor.

In FY 1997, FDA's actual obligations for the process for the review of human drug applications, excluding obligations paid from user fees, was $147,959,689, as reported in the

FY 1997 Financial Report to Congress. Multiplying this amount by the adjustment factor of 1.1042 derived above, FDA's 1997 adjusted minimum spending for the process for the review of human drug applications from appropriations, exclusive of fees, $163,377,089 in FY 2002.

The FDA costs (obligations) from appropriations for the process for the review of human drug applications for FY 2002 was $185,815,399. Since this is greater than the adjusted FY 1997 amount ($163,377,089) the third condition was met.

The table below shows amounts FDA spent on the process for the review of human drug applications in FY 2001 and 2002 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

	Adjusted FY 1997	FY 2001	FY 2002
From Appropriations	$163,377,089	$162,691,657	$185,815,399
From User Fee Revenues		$160,713,000	$161,812,100
Total Obligations		$323,404,657	$347,627,499

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 1998, 1999, 2000, 2001, and 2002, and pending waiver requests for fees payable from the same periods.

EXEMPTIONS AND WAIVERS AS OF SEPTEMBER 30, 2002

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

Exempted Application Fees [1]

	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	
Orphan Product	16.0	14.5	16.3	14.5	10.0	
Pediatric Supplements	8.0	5.3	12.6	19.0	4.5	2
Previously Submitted					7.5	3
Total Exemptions	24.0	19.8	28.9	33.5	22.0	
TOTAL_-Exemptions Granted	**$6,164,304**	**$5,377,570**	**$8,250,743**	**$10,373,175**	**$6,893,040**	

Waivers Granted

	FY 1998	FY 1999	FY 2000	FY 2001	FY 2002	
APPLICATIONS [1]						
Small Business Waivers	15.0	7.0	8.3	12.0	6.0	4
Miscellaneous Waivers	5.0	4.5	8.3	10.3	1.0	5
Value of Waivers Approved	$5,136,920	$3,131,243	$4,492,653	$6,058,275	$1,905,974	
PRODUCTS:						
Waivers Approved	53.0	24.0	19.0	17.9	10.0	
Value of Waivers Approved	$948,009	$440,736	$379,221	$391,867	$216,300	
ESTABLISHMENTS:						
Waivers Approved	20.0	12.5	11.5	10.4	7.3	
Value of Waivers Approved	$2,329,436	$1,604,795	$1,636,926	$1,516,242	$1,028,876	
TOTAL--Waivers Granted	**$8,414,365**	**$5,176,774**	**$6,508,800**	**$7,966,383**	**$3,151,150**	

Waivers Pending Decisions

	FY 1993 Through FY 1998	FY 1999	FY 2000	FY 2001	FY 2002
APPLICATIONS:					
Waivers Pending				0	
Allowance for Pending Waivers		$0	$0	$0	
PRODUCTS:					
Waivers Pending	4	6.0	4.0	7.0	12.0
Allowance for Pending Waivers	$68,373	$110,184	$79,836	$153,244	$259,560
ESTABLISHMENTS:					
Waivers Pending	1.5	1.5	2.0	5.3	6.3
Allowance for Pending Waivers	$206,283	$192,653	$283,942	$766,442	$875,681
TOTAL--Waivers Pending	**$274,656**	**$302,837**	**$363,778**	**$919,686**	**$1,135,241**

Total Pending for all years: $2,996,198

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, PDUFA II, and the related House of Representatives Report 102-895 ("House Report"), defines the process for the review of human drug applications and the costs which may be included in that process. Using these definitions (and further refinements 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

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 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 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 within the centers. Most FDA components involved in the human drug review process perform a mixture of activities--some included in the definition of the process for the review of human drug applications, and some not included. These components fall into three categories: 1) review and laboratory components; 2) indirect review and support components; and 3) user fee excluded components. Costs are accumulated by cost centers. The allocation of costs for the three categories and center-wide expenses are discussed below.

Review and Laboratory Components:

The review and laboratory components, as organized during FY 2002, have the primary responsibility for the review of human drug applications and supplements. Below is a list of these direct review and laboratory components in CDER and CBER.

REVIEW AND LABORATORY COMPONENTS

CDER	CBER
Office of the Center Director	Office of the Center Director
Office of Medical Policy	Veterinary Services
Division of Drug Marketing, Advertising, and Communications	Regulations and Policy Staff
Division of Scientific Investigations	Quality Assurance Staff
Office of New Drugs	Office of Biostatistics and Epidemiology
Office of Drug Evaluation I	Biostatistics
Neuropharmacological Drug Products	Epidemiology
Oncologic Drug Products	Office of Blood Research and Review
Cardio-Renal Drug Products	Emerging Transfusion Transmitted Diseases
Office of Drug Evaluation II	Hematology
Metabolic and Endocrine Drug Products	Blood Applications
Pulmonary and Allergy Drug Products	Office of Therapeutics Research and Review
Anesthetic, Critical Care and Addiction Drug Products	Cellular and Gene Therapies
Office of Drug Evaluation III	Monoclonal Antibodies
Gastro-Intestinal and Coagulation Drug Products	Clinical Trial Design and Analysis
Reproductive and Urologic Drug Products	Application Review and Policy
Medical Imaging and Radiopharmaceutical Drug Products	Therapeutic Proteins
Office of Drug Evaluation IV	Office of Vaccines Research and Review
Anti-Viral Drug Products	Bacterial, Parasitic and Allergenic Products
Anti-Infective Drug Products	Viral Products
Special Pathogens and Immunologic Drug Products	Vaccines and Related Product Applications
Office of Drug Evaluation V	Office of Compliance and Biologics Quality
Anti-Inflammatory, Analgesic, and Ophthalmologic Drug Products	Manufacturing and Product Quality
Dermatologic and Dental Drug Products	Case Management
Over-the-Counter Drug Products	Inspections and Surveillance
Office of Biostatistics	
Quantitative Methods and Research Staff	
Division of Biometrics I, II, and III	
Office of Pharmaceutical Science	
Office of New Drug Chemistry	
Microbiology Team	
Division of Chemistry I, II, III	
Office of Clinical Pharmacology and Biopharmaceutics	
Division of Pharmaceutical Evaluation I, II, III	
Office of Testing and Research	
Laboratory of Clinical Pharmacology	
Division of Applied Pharmacology Research	

Division of Product Quality Research	
Division of Pharmaceutical Analysis	

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

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

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

User Fee Excluded Components

Based on a review of a component's activities and the definitions in the Act, some organizations within the centers were completely excluded from the calculation of costs related to the process for the review of drug applications. An example of a user fee excluded component is the Office of Generic Drugs in CDER. In CBER, all cost centers perform some PDUFA work, although it can be as little as 5 percent.

Center-wide Expenses

A number of center-wide expenses are collected in central accounts rather than being charged directly to a specific division. These costs include rent, utilities, some computer equipment, facilities repair and maintenance, and extramural and service contracts. Many of these costs could be traced back to the specific division that generated the cost and were assigned the user fee related percentage calculated for the division to which the expenditure related. For the costs that benefited the center as a whole and could not be traced to a specific division, a weighted average user fee percentage was calculated based on the level of user fee related costs to total costs in the center.

CENTER TIME REPORTING ENHANCEMENTS

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

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

Beginning in FY 1996, the CBER time reporting system was enhanced to collect on-line time reports for all employees for a two-week period each quarter of the year. The enhanced system reports time for 70 possible functional activities, by 10 product classes.

In November 1997, CDER initiated an on-line time reporting survey of each employee within the Center. Beginning in FY 2001, this survey captures the expenditure of time on PDUFA-

related activities and all other CDER mission-oriented activities for two four-week periods—one in each half of the fiscal year.

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 was complete in FY 2001. The remaining research related to drug review is now supported solely 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.

CENTER TIME REPORTING RESULTS FOR FY 2002

The time reporting systems operated by CBER and CDER indicated the 66 percent of all time spent in CBER and 74 percent of all time spent in CDER in FY 2002 was dedicated to the process for the review of human drug applications as defined in PDUFA.

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. 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 for the FY's 2001 and 2002, respectively.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS
as of September 30, 2001 and 2002

Cost Component	FY 2001	FY 2002
Staff Years Utilized	180	153
ORA Average Salary & Benefits	$74,670	$77,987
Salary and Benefits	$13,440,656	$11,931,986
Operations and Rent	$8,807,063	$7,268,883
Total	**$22,247,719**	**$19,200,869**

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 substantial 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 decrease in the number of new drug and biologic applications in FY 2001 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 2002, 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 Science Coordination and Communication
- Office of Communications and Constituent Relations
- 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, $25,773,229 and $28,563,982 in general and administrative obligations were dedicated to the human drug review process in FY's 2001 and 2002, respectively. These are total costs, including funds obligated both from appropriations and from fees. The Agency general and administrative obligations in FY 2002 accounted for about 8.2 percent of the total FY 2002 cost of the process for the review of human drug applications. This is up slightly from 8.0 percent in FY 2001, but is still 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 21 percent since 1998. This remarkable sustained reduction in overhead is the result of FDA's commitment to increase efficiency in its operations.