



PDUFA II

Five-Year Plan

FY 1999 Revision

1998 - 1999 - 2000 - 2001 - 2002

Department of Health and Human Services
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Executive Summary

The Prescription Drug User Fee Act of 1992 (PDUFA I) provided substantial additional resources and staffing that enabled FDA to accelerate its drug evaluation process without compromising review quality. The Food and Drug Administration Modernization Act (FDAMA) of 1997 amended PDUFA I and extended it through September 30, 2002 (PDUFA II). PDUFA II also commits FDA to faster review goals for some applications, new goals for meetings and dispute resolution, and the electronic receipt and review of applications by 2002.

In July 1998, FDA completed the original PDUFA II Five-Year Plan, which was FDA's blueprint for investing the resources expected under PDUFA II. It was based on the planning efforts of the three FDA components directly responsible for meeting these goals: (1) the Center for Drug Evaluation and Research (CDER), (2) the Center for Biologics Evaluation and Research (CBER), and (3) the Office of Regulatory Affairs (ORA). This is the first annual revision of that plan. The major changes from the original plan are summarized below:

- Assumptions have been significantly revised, based on a more conservative projection of PDUFA fee revenue. The estimate of revenue expected over the 5 years is reduced from \$740 million to \$681 million (a reduction of \$59 million). This new revenue estimate is based on the regression analysis used to set FY 1999.
- CDER's revised plan calls for:
 - an increase of only 101 FTE's by the end of 5 years (scaled back from an increase of 240 FTE's in the original plan), with costs for additional staff and operating support to enhance the review process over the 5 years reduced from \$103 million to \$80 million, and
 - IT expenditures over the 5 years reduced from \$61 million to \$54 million.
- CBER's revised plan calls for:
 - a net increase of only 37 FTE's by the end of 5 years (scaled back from an increase of 57 additional FTE's in the original plan), with costs for additional staff and operating support to enhance the review process over the 5 years reduced from \$25 million to \$18 million; and
 - IT expenditures over the 5 years reduced from \$34 million to \$30 million.
- ORA's revised plan calls for:
 - a reduction of 40 FTE's over the 5 years (rather than an increase of 28 FTE's in the original plan), with costs for additional staff and operating support over 5 years reduced by \$17 million (largely a result of increasing reliance on record reviews in lieu of on-site pre-approval inspections); and
 - IT expenditures over 5 years remain the same in both plans--\$3 million.

Of the total planned, 56 percent will go for pay and benefits—down slightly from 58 percent originally planned. This will fund 98 more FTE's for the drug review process than were actually expended in 1997 (compared with 325 more in the original plan), or 757 more FTE's for the drug review process than were actually expended in 1992 (compared with 983 more in the original plan). Resource constraints may make meeting PDUFA triggers and goals more difficult in out-years.

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Purpose

This plan sets out, in broad terms, the five-year blueprint for investing the substantial resources FDA expects to collect under the Prescription Drug User Fee Act (PDUFA), as amended and extended by the Food and Drug Administration Modernization Act of 1997 (FDAMA). FDA must ensure that these resources are used to meet challenging new goals associated with PDUFA. The plan will help ensure that resources are used to achieve these goals. It allocates the resources expected each year among the FDA components responsible for achieving PDUFA goals.

The plan was originally developed in Fiscal Year (FY) 1998 and made available in July 1998. Annual reviews will be conducted and adjustments made as actual changes in workload and revenues replace original estimates, unanticipated contingencies occur, and new technologies develop. This FY 1999 revision of the plan is the first update of the original plan.

Background

PDUFA I

The Prescription Drug User Fee Act of 1992 provided FDA with increasing levels of resources for the review of human drug applications. Fees that FDA collected from drug and biologic firms, 1993 through 1997, were used to reduce the evaluation time for certain human drug applications without compromising review quality. Letters from the Commissioner of Food and Drugs to Congressional Committee Chairmen detailed these goals. By 1997, these fees were providing FDA with an additional \$87.5 million a year to devote to the drug evaluation process.

FDA primarily spent these new resources to acquire personnel to review human drug applications and to update the information technology (IT) infrastructure supporting the human drug review process. FDA staff dedicated to these reviews in the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Office of Regulatory Affairs (ORA) increased over 57 percent during this period--from 1,147 staff-years in 1992 before PDUFA was enacted to 1,806 staff-years by 1997. FDA has submitted annual Performance and Financial Reports to Congress on progress in meeting performance goals and the use of fees.

The growing recognition of FDA's success in ensuring that these resources were well used culminated in late 1997 when FDA received the prestigious Innovations in American Government Award, jointly sponsored by the Ford Foundation and the Harvard University John F. Kennedy School of Government, in partnership with the Council for Excellence in Government. This award honored FDA's achievement in combining user fees and management principles to develop a new drug approval process that is predictable, accountable, and scientifically sound while making safe and effective drugs available to the public more quickly.

PDUFA contained a "sunset" provision for automatic expiration on September 30, 1997. Without further legislation, FDA would have been unable to continue to collect and spend PDUFA fees essential to maintain the review process improvements after that date.

PDUFA II

Congress worked with the regulated industry and the Administration to ensure PDUFA's continuation. As a result, the FDAMA was signed by President Clinton on November 21, 1997. Subtitle A of Title 1 of FDAMA amended PDUFA and extended it through September 30, 2002. This extension authorizes funds that will enable FDA to accomplish increasingly challenging goals over this five-year span. These new goals were set forth in letters from the Secretary of Health and Human Services to Congressional Committee Chairmen on November 12, 1997. PDUFA, as amended and extended by FDAMA and with its new goals, is referred to as PDUFA II and its predecessor is now referred to as PDUFA I.

PDUFA II authorizes appropriations that will provide FDA with resources to sustain the larger drug review staff developed in the last 5 years and to achieve the even more stringent new goals.

New Goals

The new goals of PDUFA II are enormously challenging, diverse, and resource intensive. Major components of the review process will be accelerated further. Many of the goals will require the development and issuance of guidance documents and data bases to track and report performance. Goals are established in totally new areas, such as meetings with industry and dispute resolution. The development of infrastructure and tools necessary to move to electronic application receipt and review will also be essential. The following table provides an overview and comparison of the major goals by the end of PDUFA I and the end of PDUFA II. (For more detail on the actual goals and FDA's performance, see FDA's latest Performance Report submitted to Congress in December 1998.)

Comparison of Goals at the End of PDUFA I and PDUFA II

Goal	PDUFA I	PDUFA II
Complete review of priority original new drug applications and efficacy supplements	90% in 6 months	90% in 6 months
Complete review of standard original new drug applications and efficacy supplements	90% in 12 months	90% in 10 months
Complete review of manufacturing supplements	90% in 6 months	90% in 4 months if prior approval needed
Complete review of resubmitted new drug applications	90% in 6 months	90% of class 1 in 2 months and 90% of class 2 in 6 months
Respond to industry requests for meetings	No Goal	90% within 14 days
Meet with industry within set times	No Goal	90% within 30, 60, or 75 days, depending on type of meeting
Provide industry with meeting minutes	No Goal	90% within 30 days
Communicate results of review of complete industry responses to FDA clinical holds	No Goal	90% within 30 days
Resolve major disputes appealed by industry	No Goal	90% within 30 days
Complete review of special protocols	No Goal	90% within 45 days
Electronic application receipt and review	No Goal	In place by 2002

FY 1999 Revision

When the PDUFA II Five-Year Plan was originally published in July 1998, FDA committed to annual reviews and adjustments as actual changes in workload and revenues replace original estimates, unanticipated contingencies occur, and new technologies develop. This FY 1999 revision is the first update since the original plan was developed and published. Four of the assumptions in the next section have changed significantly in this revised plan as a result of our experience through the end of FY 1998, and annual revenue forecasts and expenditure plans are reduced.

One of the new features included in PDUFA II was a workload adjuster. Its purpose was to assure that fee revenues would increase proportionally with increases in workload. Likewise, when workload decreased, revenues would decrease. FDAMA made the number of fee-paying applications the surrogate for PDUFA workload.

In FY 1998, the number of applications submitted to FDA for review declined for the first time in 6 years, as noted in both the FY 1998 PDUFA Performance Report released in December 1998 and in the FY 1998 PDUFA Financial Report released in February 1999. FDAMA amendments exacerbated this decline, causing over 30 more applications to be exempt from fees than would have been exempt previously. Thus, there was a substantial decline in the number of fee-paying applications in FY 1998.

Total PDUFA workload, which includes the increasing volume of items exempt from fees as well as an increasing volume of work not subject to fees--such as investigational new drug submissions and manufacturing supplements--increased in FY 1998. Unfortunately, the PDUFA II workload adjuster does not reflect real changes in PDUFA workload.

FDA published a *Federal Register* notice on December 22, 1998, stating the number of fee-paying submissions received in FY 1998, and explaining that the past approach to estimating fee-paying applications for FY 1999 (based on the actual number received in the immediately preceding year) would be problematic. In that notice, FDA used linear regression analysis to estimate the number of fee-paying applications and application fee revenues for FY 1999. The notice also set product and establishment fees based on this forecast. Using that same method to estimate fee-paying applications and revenues through FY 2002, this plan revision significantly lowers the forecast of fee revenues through 2002, and expenditure plans are similarly scaled back.

Assumptions

Taking advantage of experience gained during PDUFA I and experience through FY 1998, this revised plan is based on ten major assumptions. Each of the assumptions was reassessed for FY 1999. Most are unchanged or have very minor revisions. However, assumptions 2, 4, 8, and 9 have been significantly revised, based on a more conservative projection of fee revenues. A discussion of all ten assumptions follows.

1. As in the original plan, the increases funded by PDUFA I will be maintained over the course of PDUFA II.

The fees collected during PDUFA I funded activities that became an integral part of FDA's resources for reviewing human drug applications. In 1997, two-thirds of these funds were spent on pay and benefits for an additional 659 Full Time Equivalents (FTE's) above the level of effort FDA was expending on the review of human drug and biologic applications in 1992. The remaining one-third of the funds was used to provide operating support, IT support, centrally funded support (for indirect costs such as utilities and telecommunications), rent, and overhead costs. The continuation of these 659 work-years of effort in the centers and ORA is crucial to FDA's ability to review drug and biologic applications rapidly. These resources are the foundation for building improvements mandated by PDUFA II.

PDUFA II ensures that these additional human resources (referred to as the PDUFA I additive base FTE's) continue to be dedicated to the drug review process over the next 5 years. They are allocated as follows:

PDUFA I Additive Base FTE's by Component

Year	CDER	CBER	ORA	Total
1998	398	187	74	659
1999 and Beyond	418	167	74	659

Adjustments in these allocations may be made if warranted by workload changes.

The 5-year estimated costs associated with these PDUFA I additive base activities are detailed in the table on the next page and reflect:

- Annual pay and benefit cost increases of 5 percent (based on 5 years' experience).
- Center support costs of \$9,000 per FTE annually. These are base costs and exclude past allocations for specific projects or needs.
- ORA's support costs of \$16,000 annually per FTE (largely due to ORA's travel costs for pre-approval inspections).
- Center support cost estimates also include research support funds for CBER of \$590,000

in 1998 and \$295,000 in 1999 (discontinued after 1999).

- Overhead calculated as a percent of center/ORAs pay and benefits (a formula prescribed by the Office of the Assistant Secretary for Finance and found reasonable by Arthur Andersen, a major accounting firm, and validated by Inspector General audits).
- Central account and rent estimates are based on 1997 actual costs and inflated at 5 percent annually, based on experience over the past 5 years.

PDUFA I Additive Base Fund Estimates (\$000)

Item	1998	1999	2000	2001	2002	*Total
Pay and Benefits for 659 Center/ORAs FTE's	\$61,366	\$65,219	\$68,480	\$71,904	\$75,499	\$342,469
Center/ORAs Support	\$7,021	\$6,726	\$6,431	\$6,431	\$6,431	\$33,040
Overhead	\$10,889	\$10,957	\$11,505	\$12,080	\$12,684	\$58,114
Central Accounts	\$4,230	\$4,642	\$4,864	\$5,097	\$5,342	\$24,173
*Total	\$83,506	\$87,544	\$91,280	\$95,512	\$99,956	\$457,797

*Numbers may not add due to rounding.

2. Fee revenue estimates are based on annual increases of about 5 percent in fee-paying applications (rather than 7 percent as assumed in the original plan) and inflation increases of 3 percent. This revision reduces the estimated revenue over 5 years by over \$62 million.

During discussions leading to the enactment of PDUFA II, both industry and FDA participants focused on the largely unanticipated increase in application review workload during PDUFA I and the need to ensure increasing revenues if this trend continues in PDUFA II. The following table, derived from the *Federal Register* Notices FDA published each year as a part of its fee-setting process, summarizes the increasing workload.

PDUFA Fee-Paying Full Application Equivalent Estimates by Year

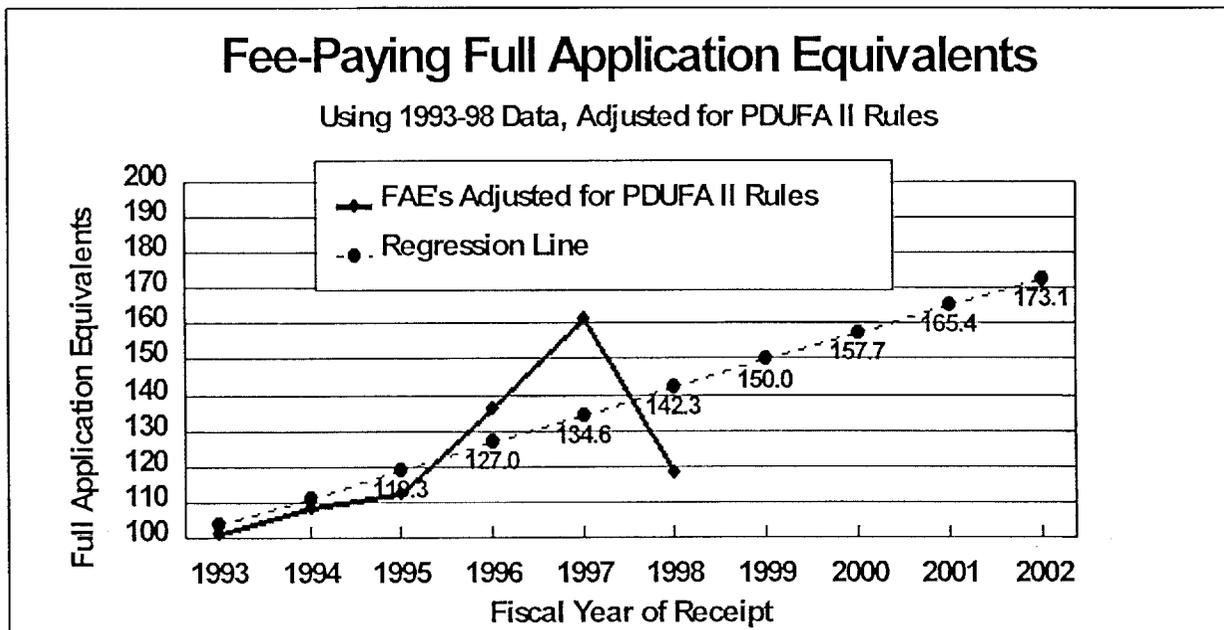
Fiscal Year	Full Application Equivalents	Percent Change from Previous Year	Allowance for Waivers or Reductions	Basis for Next Year's Fees	Percent Change from Previous Year
1993	116			116	
1994	129	11.2%	5	124	6.9%
1995	137	6.2%	6	131	5.6%
1996	157	14.6%	16	141	7.6%
1997	192	22.3%	40	152	7.8%

Based on this information (excluding 1997 data unavailable during discussions that led to PDUFA II) negotiators agreed that it was reasonable to include a workload adjustor in PDUFA II. The adjustor would cause FDA resources to increase or decrease as the workload fluctuated. The statute was crafted so that FDA fee revenues would increase in any year FDA anticipated receiving more than 142 fee-paying full application equivalents (the number used to set the fee level each year in the statute) and decrease in any year FDA anticipated receiving less than 142 fee-paying full application equivalents.

As part of these negotiations, FDA analyzed the effect of both increasing and decreasing workload levels and inflation. Industry and FDA negotiators agreed that the most reasonable planning scenario was a continued yearly increase in fee-paying application workload of 7 percent and inflation of 3 percent. These assumptions were the basis for projecting both revenues and workload in the original plan of July 1998.

In 1998, FDA received only 119 fee-paying full application equivalents, considerably below the 152 fee-paying full application equivalents estimated in the December 9, 1997 *Federal Register* notice. In light of this shortfall, the original projections above have been revised.

FDA published a *Federal Register* notice on December 22, 1998 (Attachment 1), using linear regression analysis to estimate the next year's number of fee paying applications and application fee revenues. Using that same method to estimate fee-paying applications and revenues through FY 2002 projects an increase of about 5 percent each year, as depicted in the graph below:



Based on the regression line shown above, FDA developed a projection of fee revenues that is included in Attachment 2. The following table summarizes the revised projection and how it differs from the original projection in July 1998.

Planned PDUFA Fee Collections by Year--Original, Now, and Difference (\$000)

Item	1998	1999	2000	2001	2002	Total
Fees--Original Plan	\$117,122	\$132,273	\$145,435	\$167,168	\$177,915	\$739,913
Fees--Current Plan	\$117,122	\$122,527	\$132,934	\$149,273	\$155,691	\$677,547
Difference		(\$9,746)	(\$12,501)	(\$17,895)	(\$22,224)	(\$62,366)

As a result of this reassessment of potential revenues through FY 2002, this revised five-year plan assumes that revenue collections will be \$62 million less than originally planned. The expenditures in this plan have been scaled back accordingly.

3. As in the original plan, each year FDA will spend approximately the same amount it collects in fees, maintaining an adequate carryover balance at the end of each year.

If FDA spends approximately as much as it collects each year, all of the PDUFA II revenues collected over the 5 years will be used. This assumption is possible because FDA began PDUFA II with a carryover balance--the PDUFA fees FDA collected but did not obligate by the end of the fiscal year and which are "carried over" for use in a future fiscal year. At the end of FY 1998, the carryover cash amounted to about \$67.5 million. If FDA spends approximately the amount it collects each year, a similar carryover balance will continue at the end of each fiscal year. A carryover balance is necessary at the end of each 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 estimating purposes, this portion is distributed evenly over 12 months. These application fees in aggregate would cover FDA costs for 1 1/3 months of the first 4 months of the fiscal year. FDA needs to carry forward at least 2 2/3 months of operating costs into each new fiscal year to cover expenses until the product and establishment fees are received on January 31. In addition, because PDUFA contains provisions that could prevent FDA from being able to assess or collect fees (specified minimum levels that must be available from traditional appropriations), FDA has to maintain some reserves to cope with shut-down contingencies in any year. (Carryover balances are discussed further on pages 24-25.)

4. About \$220 million will be available over 5 years for PDUFA II increases, rather than the \$284 million estimated in the original plan.

If the total amount needed to sustain the PDUFA I initiatives derived under Assumption 1 is subtracted from the total revenues FDA expects to have available each year under Assumption 2, the net available for allocation to meet the PDUFA II goals is derived. Net available is the increment available to FDA over and above the PDUFA I additive base resources already

invested to support and maintain the 659 additional FTE's in the centers and ORA. This is the amount available for additional investments over the next 5 years to meet the PDUFA II goals.

Revenues Anticipated and Net Available for Allocation (\$000)

Item	1998	1999	2000	2001	2002	Total
Fees Anticipated	\$117,122	\$122,527	\$132,934	\$149,273	\$155,691	\$677,547
PDUFA I Additive Base	\$83,506	\$87,544	\$91,280	\$95,512	\$99,956	\$454,343
Net Available	\$33,616	\$34,983	\$41,654	\$53,761	\$55,735	\$219,750

This represents about a 23 percent reduction from the amount planned in July 1998. Most of the reductions are achieved by reducing planned staffing levels. Information technology expenditures are only slightly reduced, in order to achieve electronic receipt and review of applications by the end of FY 2002.

5. As in the original plan, all statutory conditions necessary for PDUFA to operate will be met each year.

The law allows FDA access to PDUFA II revenues only if three conditions are met. This plan assumes the following statutory conditions will be met:

- FDA appropriations (exclusive of user fees) in future years must total at least as much as FDA received in 1997, with some adjustments.
- Each year FDA must spend at least as much from appropriated funds (exclusive of user fees) on the human drug review process as it spent from appropriations (exclusive of user fees) on this process in 1997--with some adjustments.
- PDUFA fee revenues may be collected and spent only to the extent provided each year in FDA's appropriation.

6. As in the original plan, funds planned for acquiring human resources may be spent on either hiring or contracting.

To develop cost estimates, it was assumed that human resources would be acquired by hiring additional employees. The centers and ORA should not feel constrained in how necessary additional human resources are acquired. They are encouraged to utilize contract support any time it is more practical or cost effective than hiring.

7. As in the original plan, the amount FDA pays for rent for PDUFA and other programs will no longer be capped beginning in FY 1999.

For a substantial period before FY 1992, and continuing through FY 1998, FDA's Appropriation Act maintained a cap on the amount of rent FDA could pay the General Services Administration

(GSA). As a result, since there was no increase in rent costs from FY 1992 through FY 1998, PDUFA fees were not used to pay for GSA rent--the flat GSA rent payments were all a part of the PDUFA appropriated base.

The FY 1999 Appropriation Act for FDA no longer contains that cap and requires FDA to pay full GSA rent charges just as all other government departments and agencies do. With the removal of the cap, the total amount of rent that FDA will pay to GSA will almost double--increasing from \$46.3 million in FY 1998 to \$88.3 million in FY 1999. This will impact all programs, including the human drug review process. The share of rent payable for the human drug review process will increase by \$5.4 million. This plan assumes that rent costs after FY 1999 will increase with inflation (3 percent annually).

Estimated Rental Payments for Human Drug Review Process (\$000)

Rent Paid to GSA	1998	1999	2000	2001	2002
From Rent Appropriation	\$6,466	\$6,559	\$6,704	\$6,858	\$7,016
From PDUFA Fees	\$0	\$5,428	\$5,643	\$5,859	\$6,083
Total Rent Paid to GSA	\$6,466	\$11,987	\$12,347	\$12,717	\$13,099

8. **A small but increasing amount will be held in a contingency reserve each year after 1999--almost double the amount in the original plan.**

The likelihood that unanticipated events will occur increases each succeeding year of the plan. To cope with these events, a small but increasing amount will be held in a contingency reserve each year after 1999. One such contingency is utility costs that FDA did not have to pay in 1997 and earlier but may have to pay in the future. However, these contingency reserves are being kept to a minimum in order to allocate as much of the planned revenue to the centers and ORA as possible to implement their plans. All funds anticipated during FY 1998 and FY 1999 are allocated in the plan.

Contingency reserves of \$3 million, \$4 million, and \$7 million are planned for fiscal years 2000, 2001, and 2002, respectively. These contingency reserves have been almost doubled from the total in the original plan to help the agency cope with revenue uncertainty inherent in PDUFA II. Potential claims on this reserve will be assessed in the second quarter of each fiscal year and allocations will be made. Funds not required for contingencies will then be allocated among CDER, CBER, and ORA for PDUFA needs.

9. **Over the course of PDUFA II, total funding from all sources for the human drug application review process should increase by about 36 percent, rather than by 45 percent as originally estimated.**

The above assumptions permit a projection of revenues available for the review of human drug

applications through 2002--shown in the chart below. The revenues resulting from PDUFA II will allow program funding to increase by about 36 percent over the 5 years of this program--from \$232 million in 1997 to \$316 million in 2002. At first this may appear large. Average salary and benefit costs alone, which account for well over half of all costs, are expected to increase by about 28 percent by the end of 5 years--the compounded result of an average increase of 5 percent each year. This leaves a rather modest increase for other costs--particularly in light of the very intense investment in information technology required to achieve the PDUFA II goal of electronic receipt and review of applications by the end of FY 2002. Thus, this revised plan reflects substantially fewer additional employees than the original plan.

Viewed from another perspective, this increase is less than the compounded increase in workload (5 percent) and inflation (3 percent) that forms the basis of the revenue projections. Workload and inflation increases alone, when compounded, exceed 47 percent over 5 years. And inflation at 3 percent really understates the costs of inflation that FDA expects to experience, since pay and benefit increases have historically been at substantially higher levels (5 percent).

This PDUFA II 5-year plan revision is based on the total revenue stream shown in the table below.

Projection of Funds Available for the Human Drug Application Review Process (\$000)

Source of Funds	1997 Actual	1998 Estimate	1999 Estimate	2000 Estimate	2001 Estimate	2002 Estimate
S&E Appropriations	\$141,493	\$141,493	\$143,525	\$146,682	\$150,056	\$153,507
Fees from Industry	\$84,289	\$117,122	\$122,527	\$132,934	\$149,273	\$155,691
Rent Appropriations	\$6,466	\$6,466	\$6,559	\$6,704	\$6,858	\$7,016
*Total Funds	\$232,249	\$265,081	\$272,611	\$286,320	\$306,187	\$316,214

*Numbers may not add due to rounding. The S & E Appropriation amounts are projections of the minimum amounts that must be spent from appropriations on the process for the review of human drug applications in order to meet the statutory requirements of PDUFA II.

10. As originally planned, the plan will be reassessed and revised annually.

All allocations in the plan are subject to review and reassessment early in each fiscal year as figures for workload and revenue for the previous year are available and better estimates for the next year's revenues are made. Of course, adjustments will have to be made based on these assessments. The plan will continue to have value as the baseline from which future changes will be made. This annual reassessment process is discussed further on page 28.

Plans

The planning process for meeting new PDUFA II goals began during discussions with industry in the last year of PDUFA I. As new goals were proposed, resource implications were also estimated and discussed. These ongoing discussions over many months resulted in the PDUFA II goal letters of November 12, 1997 and the PDUFA II resource levels and adjustors to achieve those goals that were enacted in the statute.

The PDUFA II Five-Year Plan completed in July 1998 reflected the resources FDA initially anticipated and plans for investing those resources. Responding to the reduced resources FDA now anticipates, the Deputy Commissioner for Management and Systems issued scaled-back planning targets to CBER, CDER, and ORA in December 1998. The lowered planning targets were kept in proportion to the amount for each component in the original plan of July 1998. Each component was then asked to revise its plan, keeping within the new lowered targets and assuring that PDUFA II goals would be met.

The Office of Management and Systems (OMS) worked with CDER, CBER, and ORA to integrate their plans into an overall FDA plan. The primary focus of this effort was to ensure sound plans supporting PDUFA II goals. The IT portions of each component's plan is provided in more detail in the PDUFA II Information Management Five-Year Plan--Attachment 3. This revised IT plan presents more detail than last year's plan and better explains how IT projects support one another. It also identifies Electronic Regulatory Submission and Review (ERSR) accomplishments to date.

The overall PDUFA II Five-Year Plan revision resulting from this process provides a sound framework for the investments needed to ensure FDA success with PDUFA II. The following pages summarize the planned distribution of PDUFA II funds to each component (CDER, CBER, and ORA) over the next 4 years and an FDA Plan Summary. The two largest demands continue to be: (1) additional human resources to meet the more stringent application review times under PDUFA II goals and (2) IT investments to achieve paperless application receipt and review by the end of PDUFA II.

CDER Plan Summary

CDER has developed an amended, detailed overall plan for the 5 years of PDUFA II, reflecting the revised resource level estimates. The revised plan totals \$133.3 million--a reduction of \$30.1 million over the final 4 years of the program. A year-by-year resource summary of CDER's plan is on page 15. It has the same three principal components as last year's plan: (1) personnel and support, (2) review process enhancements, and (3) information technology.

Personnel and Support

The largest portion of CDER's initial plan was for funds to hire and support additional staff for the drug evaluation process. This represented \$91.4 million (56 percent) of CDER's total plan and would have enabled CDER to add 240 more FTE's to the drug review process by FY 2002.

Confronted with the substantially reduced PDUFA revenues and continuing challenges of recruiting and retaining the highly skilled work force demanded for the medical and scientific evaluation of applications, CDER has substantially reduced the Personnel and Support component of its revised plan. This plan now reflects increasing Personnel and Support for CDER by \$45.8 million (about 35 percent of planned resources), which will support 101 additional FTE's by FY 2002 (mostly in CDER's Office of Review Management). This number is in addition to the PDUFA I additive base of 418 FTE's and CDER's appropriated PDUFA base of 749 FTE's--for a total PDUFA effort of 1268 FTE's by FY 2002.

Recognizing that it takes 12 to 24 months for new employees to become proficient reviewers, CDER will try to hire most of the new staff in fiscal years 1999 and 2000. This will allow staff to be trained and to handle the increased workload associated with PDUFA II goals and increasing workload during the final 2 years of PDUFA II.

The Personnel and Support subtotal also includes funds to acquire more space for this additional staff--\$1.8 million over the 5 years. This amount will be used to pay increased rental costs to GSA and will be held in reserve until arrangements are made for acquisition of this additional space.

Review Process Enhancements

The second component of CDER's plan is funding for a number of enhancements to the application review process. This has increased substantially from CDER's initial plan. CDER plans \$34 million (25 percent of the total plan) for this purpose through FY 2002. These improvements span many offices which directly contribute to or support the attainment of PDUFA II goals. It includes funds to: standardize and improve review practices, enhance medical library resources for reviewers, expedite the validation of methods in new drug applications, train reviewers, increase clinical trial inspections, and improve PDUFA time reporting systems, enhance support and services for the drug listing program, enhanced document management and accountability, and support for additional advisory committee meetings

essential to expedite review. Also included are estimated travel funds for International Conference on Harmonization (ICH) meetings that will promote accelerated drug development through agreements on shared standards for use in the United States, Japan, and European pharmaceutical authorities. The actual distribution of these funds will be decided each year by the Office of International and Constituent Relations which coordinates ICH activities.

Information Technology

The final component of CDER's plan is \$53.6 million (40 percent of the total) for IT enhancements for the drug review process and includes three parts: (1) funds to develop the capability for electronic application receipt and review by FY 2002 which account for \$20.7 million, (2) funds for replacing CDER's management information system which account for \$9 million, and (3) funds for many other IT enhancements that support the PDUFA II goals (such as replacement of one-third of the personal computers of the reviewers every 3 years and overall maintenance and upgrading of CDER's data systems and networks that support PDUFA) which account for \$18.5 million over 5 years. The CDER IT reserve also includes another \$5.3 million that is tentative, pending further discussion with FDA's Office of the Chief Information Officer (OCIO).

The IT goals for PDUFA remain fixed and this part of CDER's plan has changed the least from last year.

The IT part of the plan was compared to industry practices and standards utilizing outside contract support. As a result, some adjustments were made and other amounts are held in reserve until more complete plans for their use are agreed to between CDER and the OCIO. The OCIO will advise CDER on how funds held in reserve can be released and any other clearance processes for planned funds for IT projects.

The table on the following page summarizes CDER's revised plans to invest the additional funds made available as a part of PDUFA II. The table at the bottom of the following page summarizes the total PDUFA funds added to CDER each year. The first three lines show the amounts to support the PDUFA I additive base funds. The fourth line shows the total PDUFA II plan request and the last line shows the total of the PDUFA fee revenues planned for CDER each year.

FY 1999 Five-Year Plan Revision

CDER Plan Summary Tables--PDUFA II
Plan for Funds in Addition to PDUFA I Additive Base (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
PDUFA Additive FTE's Base	398	418	418	418	418	
PDUFA Additive FTE's in This Plan (1)	421	479	509	519	519	
Additional FTE Requested (Cum) (Increment Each Year)	23 23	61 38	91 30	101 10	101	
Additional FTE Payroll (2)	\$1,954	\$5,464	\$8,559	\$9,974	\$10,473	\$36,423
Operating Support for Additional FTE's (3)	\$207	\$549	\$819	\$909	\$909	\$3,393
Startup Costs for New FTE (One-time) (4)	\$219	\$361	\$285	\$95	\$0	\$960
Recruit/Relocation/Renos/Security	\$1,221	\$550	\$500	\$500	\$500	\$3,271
OMS Reserve for Additional Space		\$305	\$455	\$505	\$505	\$1,770
Subtotal--Personnel and Support	\$3,600	\$7,229	\$10,618	\$11,983	\$12,387	\$45,817
ICH Support (5)	\$420	\$365	\$420	\$420	\$420	\$2,045
Redesign of Sci. Review Process	\$3,392	\$8,144	\$6,926	\$6,739	\$6,760	\$31,961
Subtotal--Process Enhancements	\$3,812	\$8,509	\$7,346	\$7,159	\$7,180	\$34,006
Electronic Submissions	\$4,979	\$4,545	\$4,846	\$3,245	\$3,115	\$20,730
Document Management	\$1,772	\$2,966	\$2,053	\$1,134	\$1,135	\$9,060
Other Electronic Initiatives (6)	\$4,998	\$4,488	\$3,619	\$2,685	\$2,740	\$18,530
Reserve Pending OIRM Approval (7)	\$939	\$0	\$2,050	\$1,150	\$1,150	\$5,289
Subtotal--Information Technology	\$12,688	\$11,999	\$12,568	\$8,214	\$8,140	\$53,609
Total Plan--CDER	\$20,100	\$27,737	\$30,532	\$27,356	\$27,707	\$133,432

- (1) PDUFA Additive FTE Base (preceeding line) plus Net Additional FTE included in this plan.
- (2) Salary and benefits estimated at \$85,228 in 1998 and escalated at 5% annually thereafter. The 1998 amount is reduced by 75% for a July 1 estimated on-board date.
- (3) Operating Support per FTE is calculated at \$9,000 per year.
- (4) \$9,500 per FTE is provided in first year only for start-up costs.
- (5) Estimate only: Actual distribution of ICH funds will be decided each year by the Office of External Affairs.
- (6) Includes \$150,000 for enhancing either CDER or ORA automated system for tracking bioresearch monitoring inspections
- (7) Funds in this line include potential upgrades for CDER systems. These reserves will be released after the FDA Chief Information Officer has approved their use.

Total Additive PDUFA Funds for CDER--Base and Plan (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
Base Payroll for 418 FTE's (5% Inflation) *	\$40,517	\$44,532	\$46,758	\$49,096	\$51,551	\$232,455
Base Operating Funds	\$3,582	\$3,762	\$3,762	\$3,762	\$3,762	\$18,630
Subtotal--Base Allotment	\$44,099	\$48,294	\$50,520	\$52,858	\$55,313	\$251,085
Total for PDUFA II Five-Year Plan	\$20,100	\$27,737	\$30,532	\$27,356	\$27,707	\$133,432
Total PDUFA Additive Funds--CDER	\$64,199	\$76,031	\$81,052	\$80,215	\$83,020	\$384,517

* Payroll Base is for 398 FTE's in 1998 and 418 Each Year Thereafter (20 FTE's Transferred from CBER)

CBER Plan Summary

CBER has developed an amended, detailed overall plan for the 5 years of PDUFA II, reflecting the revised resource level estimates. The revised plan totals \$48.4 million--a reduction of \$10.6 million over the final 4 years of the program. A year-by-year resource summary of CBER's plan is on page 18. It has the same three principal components as last year's plan: (1) personnel and support, (2) review process enhancements, and (3) information technology.

Personnel and Support

CBER had an unusually high personnel attrition rate in FY 1998. Because the PDUFA program is such an integral part of the center's activities, it caused CBER to underburn PDUFA FTE's for the first time. The unsettled nature of the FY 1999 PDUFA revenue forecast precipitated a hiring freeze early in the fiscal year for several months. This coupled with the large underburn from the previous fiscal year leads CBER to project an underburn of about 10 FTE's in FY 1999. This takes into account CBER's plan to hire an additional 15 FTE's during FY 1999, which will require operating support and start-up costs. This underburn will reduce the FY 1999 personnel and support costs by \$1 million and effectively reduce the net increase for that fiscal year to 5 FTE's.

CBER's plan is to bring on board the FTE's indicated early in PDUFA II due to the changes in the PDUFA goals, the lead-time required for new personnel to become effective reviewers, and the added tasks necessary to review these applications. CBER has a large proportion of fee-exempt and fee-waived applications that still must meet the PDUFA goals. Hiring the majority of the FTE's in the early years will allow CBER to process these applications without extreme hardship. All of the CBER FTE numbers still reflect the reprogramming of the 39 PDUFA I additive base FTE's from research into review activities (13 each year for FY 1998, 1999, and 2000) because of the PDUFA II agreement to phase out funding research with fee revenues.

In FY 2000, the final 13 FTE's will be reprogrammed from research into review work. In the revised plan, additional FTE's for FY 2000 are reduced from 6 to 3. Because of the continued lower than projected user fee revenues, FY 2001 FTE additions were reduced from 11 additional to 3 and in FY 2002, no additional FTE's are anticipated. The majority of these cuts were taken in the area of priority application review, dispute resolution, and protocol assessment.

The total funds for CBER Personnel and Support include pay and benefits for the additional FTE's and operating costs to support them. In FY 1999, the funds for acquiring space to house the additional staff has been eliminated since attrition during the previous year made space available. The reduction of staffing in future years has reduced the amount of this item in the last 3 years of the program. CBER's total payroll has been revised to \$14.4 million, 29.7 percent of the total request. It was previously 33 percent of the total.

Review Process Enhancements

CBER's reduction in the review process enhancements was more modest, and still remains 9 percent of the total plan. However, the Document Control Center funding was modified as was training due to the reduction in new hires and lower anticipated revenues. The ICH travel funds reflect projections based on FY 1998 actual amounts and the FY 1999 plan for funds. The actual distribution of these funds will be decided each year by the Office of International and Constituent Relations which coordinates ICH activities.

Information Technology

The Information Technology (IT) component was reduced by \$4.5 million but remains the largest part of CBER's plan -- \$ 29.9 million (62 percent of the total plan). The reduction in FTE's does not impact the necessity to develop and enhance the IT environment needed to meet PDUFA II goals. FY 1999 shows a slight increase in planned funds, and then a reduction in the remaining 3 years. Reductions in the IT categories of Electronic Submissions and Other Electronic Initiatives have been off-set by increases in the Document Management area.

The Electronic Submissions area will focus primarily on the establishment of CBER's Electronic Document Room. CBER will work closely with CDER on other aspects of electronic submissions (e.g., electronic signature, secure e-mail) to achieve the paperless submission environment by the end of FY 2002. For the Other Electronic Initiatives area, the decrease will result in a longer desktop replacement cycle and a more conservative network infrastructure upgrade approach.

The increase in the Document Management area will be directed toward two projects: (1) the Biologics Regulatory Management System (BRMS) and (2) the Regulatory Management System (RMS). The BRMS is CBER's existing application review management system. The RMS is the projected application review management system which will incorporate project management concepts. The RMS is an integral part of CBER's Managed Review Process. The development and implementation of RMS has been delayed. More resources are needed to add staff to the development effort. In addition, resources are required to enhance the legacy system, BRMS, until it is replaced by RMS.

The table on the following page summarizes CBER's revised plans to invest the additional funds made available under PDUFA II. The table at the bottom of the page summarizes the total PDUFA funds added to CBER each year. The first three lines show the amounts to support the PDUFA I additive base funds. The fourth line shows the total PDUFA II plan, and the last line shows the total of the PDUFA fee revenues planned for CBER each year.

CBER Plan Summary Tables--PDUFA II

Plan for Funds in Addition to PDUFA I Additive Base (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
PDUFA Additive FTE's Base	187	167	167	167	167	
PDUFA Additive FTE's in this plan (1)	203	198	201	204	204	
Total FTE's Needed to Meet PDUFA II Goals	29	57	73	76	76	
FTE's Reprogrammed from Research	-13	-26	-39	-39	-39	
Net Additional FTE Requested	16	31	34	37	37	
(Increment Each Year)	16	15	3	3	0	
Salary and Benefits for Additional FTE's (2)	\$309	\$1,733	\$2,945	\$3,366	\$3,534	\$11,887
Operating Support for Additive FTE's (3)	\$144	\$279	\$306	\$333	\$333	\$1,395
Start-up Costs for new FTE (One-time) (4)	\$152	\$143	\$29	\$29	\$0	\$352
Moves and Renovations		\$0	\$75	\$75	\$0	\$150
OMS Reserve for Additional Space			\$170	\$185	\$185	\$540
Subtotal--Personnel and Support	\$605	\$2,154	\$3,525	\$3,987	\$4,052	\$14,323
Review Process Improvements	\$976	\$1,037	\$730	\$575	\$575	\$3,893
ICH (5)	\$80	\$46	\$50	\$50	\$50	\$276
Subtotal--Process Enhancements	\$1,056	\$1,083	\$780	\$625	\$625	\$4,169
Electronic Submissions	\$1,453	\$1,360	\$668	\$599	\$599	\$4,679
Document Management	\$4,228	\$4,737	\$2,890	\$2,805	\$2,751	\$17,411
Other Electronic Initiatives	\$2,044	\$1,928	\$1,495	\$1,132	\$966	\$7,565
Reserve Pending OIRM Approval (6)	\$225	\$0	\$0	\$0	\$0	\$225
Subtotal--Information Technology	\$7,950	\$8,025	\$5,053	\$4,536	\$4,316	\$29,880
Total Plan--CBER	\$9,611	\$11,262	\$9,358	\$9,148	\$8,993	\$48,372

- (1) PDUFA Additive FTE Base (preceding line) plus Net Additional FTE Requested (bolded line below).
- (2) Salary and benefits estimated at \$82,505 in 1999 and escalated at 5% annually thereafter. The FY 1999 amount is reduced by 10 FTE, because of hiring late in the year.
- (3) Operating Support per FTE is calculated at \$9,000 per year.
- (4) \$9,500 per FTE is added only in first year for start-up costs (desk, PC, etc.).
- (5) Estimate only: Actual distribution of ICH funds will be decided each year by the Office of External Affairs.
- (6) Reserves will be released after FDA Chief Information Officer approves uses.

Total Additive PDUFA Funds for CBER--Base and Plan (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
Base Payroll for 167 FTE's (5% Inflation) *	\$15,800	\$15,320	\$16,087	\$16,891	\$17,735	\$81,833
Base Operating Funds **	\$2,273	\$1,798	\$1,503	\$1,503	\$1,503	\$8,580
Subtotal--Base Allotment	\$18,073	\$17,118	\$17,590	\$18,394	\$19,238	\$90,413
Total New Request	\$9,611	\$11,262	\$9,358	\$9,148	\$8,993	\$48,372
Total PDUFA Additive Funds--CBER	\$27,684	\$28,381	\$26,947	\$27,542	\$28,231	\$138,785

- * Payroll Base is for 187 FTE's in 1998 and 167 each year thereafter (20 FTE Transferred to CDER).
 ** Operating Base is reduced by \$295,000 in 1999 and 2000 as PDUFA additive research is phased out.

ORA Plan Summary

ORA has developed an amended plan for the 5 years of PDUFA II, reflecting the revised resource level estimates. This plan represents a major revision of last year's plan, and reflects substantial reductions in ORA resources over the remaining 4 years of PDUFA II. The table at the top of page 21 presents a year-by-year resource summary of ORA's plan. It has the same three principal components as the center plans: (1) personnel and support, (2) review process enhancements, and (3) information technology.

Personnel and Support

ORA is experiencing a marked decline in its PDUFA workload--specifically in demand for pre-approval inspections. In FY 1999 the time reported for PDUFA activities in ORA's time reporting system is decreasing, and, based on this trend, even lower levels are predicted beyond FY 1999. This results in a decrease in the use of PDUFA resources because most of the field PDUFA reimbursement formula depends on time reported in the field information system. It is difficult to predict the precise amount of time that will be reported because both the reporting and use of field time is not a linear function of time. Both assignments and reporting ebb and flow during the year.

ORA has identified several trends that appear to have caused the decline in PDUFA work. Over the last 3 years an increasing number of PDUFA decisions were based on the ORA Profiles database on establishment inspections. CDER's Office of Compliance increasingly uses field data to make decisions in lieu of requesting pre-approval inspections. District offices are also able to make PDUFA recommendations to CDER using field records, decreasing the need for PDUFA inspections. The increase in use of alternatives to inspections is a real trend.

In response to these circumstances, ORA's plan calls for 10 fewer FTE's in FY 1999, and for 40 fewer FTE's in each subsequent year. This means that staffing for ORA will fall substantially below its PDUFA I additive base of 74, so the decline in resources is reflected in negative numbers in the table on page 21. This reduction of 40 FTE's will mean that ORA will be expending a total of about 140 FTE's each year on PDUFA activities in the last year of the plan (34 FTE's paid from PDUFA fees and 106 FTE's paid from appropriations). In 2001 and 2002, as mutual recognition agreements with the European Union become effective, some of these resources will manage international agreements rather than conduct preapproval inspections.

Support costs are reduced for each FTE ORA loses in this plan revision. This reduction is \$9,000 per year (rather than the \$16,000 per ORA FTE added during PDUFA I). This lower reduction is based on the expectation of continuing and increasing international travel for preapproval inspections for remaining ORA personnel.

Review Process Enhancements

The second component of ORA's plan is \$3.5 million for enhancements to support preapproval inspection work. These enhancements include equipment, training, and better time accounting. Inadequate laboratory equipment to analyze samples collected during pre-approval inspections has delayed field completion of some pre-approval inspection work. For PDUFA II, ORA plans \$1.1 million over 5 years to purchase specific pieces of equipment required to analyze pre-approval inspection samples. ORA is also planning on \$900,000 over 5 years for PDUFA-related training. ORA's training needs are exacerbated because the 164 staff-years devoted to PDUFA in FY 1999 represent time spent by about 600 different employees. Training and refresher courses for those who conduct PDUFA pre-approval inspections or analyze samples collected have to be provided to most of these 600 individuals who contribute to the 164 FTE's of PDUFA work. The amount requested for training will meet this need. ORA's process enhancement subtotal also includes \$1.5 million to upgrade and improve its PDUFA time accounting system and to make it comparable to CDER and CBER systems. ORA's current system was designed over 25 years ago and needs to be updated.

Information Technology

The final component of ORA's plan is \$3.3 million to enable the field offices to receive and review electronic applications to enable field staff to prepare for pre-approval inspections. The requested funds will allow ORA to develop and update its information management infrastructure to allow paperless application processing.

The table at the bottom of the following page summarizes the total PDUFA funds added to ORA each year. The first three lines show the amounts to support the PDUFA I additive base funds. The fourth line shows the total PDUFA II plan request, and the last line shows the total of the PDUFA fee revenues planned for ORA each year.

FY 1999 Five-Year Plan Revision

ORA Plan Summary Tables--PDUFA II
Plan for Funds in Addition to PDUFA I Additive Base (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
PDUFA Additive FTE Base	74	74	74	74	74	
PDUFA Additive FTE in this Plan (1)	74	64	34	34	34	
Additional FTE Requested (Increment Each Year)	0	-10	-40	-40	-40	
	0	-10	-30	0	0	
Additional FTE Payroll (2)	\$0	(\$675)	(\$2,836)	(\$2,978)	(\$3,127)	(\$9,617)
Support Costs @ \$9,000/FTE	\$0	(\$90)	(\$360)	(\$360)	(\$360)	(\$1,170)
FTE Start-up Costs (3)	\$0	\$0	\$0	\$0	\$0	\$0
Subtotal--Personnel and Support	\$0	(\$765)	(\$3,196)	(\$3,338)	(\$3,487)	(\$10,787)
Equipment	\$230	\$275	\$189	\$203	\$218	\$1,115
Training	\$148	\$270	\$175	\$140	\$184	\$917
FACTS Upgrade to Monitor & Track Time		\$0	\$400	\$1,100	\$0	\$1,500
Subtotal--Process Enhancements	\$378	\$545	\$764	\$1,443	\$402	\$3,532
Electronic Submissions	\$165	\$80	\$426	\$501	\$551	\$1,723
Document Management		\$0	\$22	\$11	\$21	\$54
Other Electronic Initiatives	\$360	\$0	\$538	\$261	\$399	\$1,558
Information Technology (4)	\$525	\$80	\$986	\$773	\$971	\$3,335
Total Plan--ORA	\$903	(\$140)	(\$1,446)	(\$1,122)	(\$2,114)	(\$3,920)

- (1) PDUFA Additive FTE Base (preceeding line) plus additional FTE's included in this plan.
 (2) ORA pay and benefits based on 1999 estimate of \$67,530 per FTE increasing at 5% annually.
 (3) \$9,500 per FTE is provided only in first year an FTE is added to cover one-time start-up costs.
 (4) This line does not include \$150,000 in CDER plan for enhancing either CDER or ORA automated tracking system for bioresearch monitoring inspections.

Total Additive PDUFA Funds for ORA--Base and Plan (\$000)

Note: Numbers Are Rounded and May Not Add

Category	1998	1999	2000	2001	2002	5-Year Total
Base Payroll for 74 FTE (5% Inflation)	\$5,049	\$5,367	\$5,635	\$5,917	\$6,213	\$28,181
Base Operating Funds (3% Inflation)	\$1,166	\$1,166	\$1,166	\$1,166	\$1,166	\$5,830
Subtotal--Base Allotment	\$6,215	\$6,533	\$6,801	\$7,083	\$7,379	\$34,011
Total New Request	\$903	(\$140)	(\$1,446)	(\$1,122)	(\$2,114)	(\$3,920)
Total PDUFA Additive Funds--ORA	\$7,118	\$6,393	\$5,355	\$5,961	\$5,265	\$30,092

Overhead Summary

After the plans for CDER, CBER, and ORA were developed, the Office of Management and Systems estimated the overhead costs for PDUFA II and allocations of the overhead funds. This section provides background information on how overhead is calculated and used and summarizes plans for use in PDUFA II.

Overhead Calculation

As FDA developed PDUFA baseline costs in 1993, the Office of the Assistant Secretary for Finance prescribed the formula FDA uses to determine non-center headquarters (NCHQ) overhead costs. That formula conforms with generally accepted accounting principles and was found reasonable by Arthur Andersen consultants in subsequent annual audits. The formula is:

$$\text{Total Costs of NCHQ} \div (\text{Salary Costs of All of FDA} - \text{NCHQ Salary Costs}) = \text{Overhead Rate}$$

The salary costs used in this formula do not include any benefit costs. At the end of each fiscal year, the Office of Financial Management recalculates this overhead rate. To determine overhead costs attributable to the PDUFA activities, this rate is multiplied by the total PDUFA salary costs (excluding benefits) for CDER, CBER, and ORA. In 1998, FDA spent a total of \$253.5 million on the drug review process as defined in PDUFA, and the 1998 PDUFA overhead costs were \$26 million, or about 10¼ percent. This revised plan assumes this rate remains steady through FY 2002. In reality, recent downsizing of the Office of the Commissioner may reduce this rate, but reductions are likely to be offset by increases in center costs. The overhead costs in this revised plan decrease because fewer staff than originally planned will be hired. The FY 1999 overhead for the drug review process is estimated to be about \$26.7 million--down from \$28.4 million estimated in the original plan. Over the five year period, this plan reflects about \$8.8 million less for PDUFA overhead than the original plan.

As with all PDUFA costs, this overhead has two components: (1) a portion paid from traditional appropriations and (2) a portion paid from fees collected from industry. Under PDUFA I, the portion that must be paid from appropriations was the overhead amount FDA actually spent on this process in 1992, adjusted for cost increases since then. Under PDUFA II, the portion that must be paid from appropriations was the overhead amount FDA actually spent on this process in 1997, adjusted for cost increases since then. The adjusted overhead amount that must come from appropriations in 1999 is \$14.6 million.

The difference between the total estimated overhead costs of \$26.7 million in FY 1999 and the \$14.6 million that must be paid from appropriated funds is \$12.1 million. This \$12.1 million is the amount of FDA's overhead costs to be paid from fees. Estimates of overhead costs by fund source over the 5 years of PDUFA II are provided in the chart at the top of the next page.

Projected Drug Review Process Overhead Costs and Source (\$000)

Source	1998	1999	2000	2001	2002
S&E Appropriations	\$15,165	\$14,608	\$14,945	\$15,302	\$15,675
PDUFA Fees	\$10,889	\$12,052	\$12,961	\$13,821	\$14,512
Total Overhead	\$26,044	\$26,660	\$27,906	\$29,123	\$30,187

Use of Overhead Funds

The industry fees supporting overhead will be used in two ways: (1) direct PDUFA support, and (2) indirect support. The direct support funds will pay for specific increases to support the growth of the drug review process. The remainder is indirect support which pays for a portion of the non-center offices that provide agency-level managerial direction and support services for all FDA programs, including PDUFA.

In FY 1998, direct overhead support funded a total of 52 FTE's at a cost of \$4.9 million. These FTE's were allocated to Office of the Commissioner components whose work was directly impacted by PDUFA--such as personnel, finance, IT, facilities, contracts, and reviewing waiver requests and orphan designation requests. Over the course of PDUFA II, it is now envisioned that these direct overhead FTE's will increase to 55 by FY 2002. In addition, direct overhead funds will be allotted to the Office of the Chief Information Officer (OCIO) for information management expenses in support of PDUFA II. OCIO will be responsible for developing and maintaining the FDA electronic gateway for the receipt of electronic PDUFA applications submitted to FDA. OCIO will also develop and implement IT standards for PDUFA-related programs and provide oversight for achieving the electronic submission goal. More information about the role and costs associated with OCIO support are provided in the PDUFA II Information Management Five-Year Plan (Attachment 3). A summary of the planned allocation of direct PDUFA overhead over the course of PDUFA II follows.

Projected PDUFA Direct Overhead (\$000)

Source	1998	1999	2000	2001	2002
Direct FTE's	52	52	54	55	55
FTE Pay and Support	\$4,860	\$5,492	\$5,670	\$5,856	\$6,114
IT Support	\$438	\$691	\$1,628	\$423	\$432
Total	\$5,298	\$6,183	\$7,298	\$6,279	\$6,546

FDA Summary Plan

The Agency plan for PDUFA II is a composite of plans developed by CDER, CBER, and ORA. Tables 1-7 on pages 26 and 27 summarize the overall FDA plan. The discussion below summarizes information in each of these tables.

- Table 1 (page 26) shows the \$458 million set aside over 5 years to maintain and support the additional staff hired under PDUFA I (referred to as the PDUFA I additive base) discussed in Assumption 1. It also shows the total fee revenues expected annually and the amounts still available for enhancements after the PDUFA I additive base funds have been subtracted from the total estimated fees available--a total of about \$220 million over the 5 years.
- Table 2 (page 26) shows the allocation of \$224 million over 5 years, by component, planned to meet PDUFA II goals. (This is down from \$290 million reflected in the original plan.) The yearly amounts and totals for CDER, CBER, and ORA on the first three lines are from their individual plans. The next three lines show the amounts for: (1) overhead, (2) central accounts, and (3) rental payments to GSA. These are necessary to accommodate the additional staff hired by the centers. The next to last line shows the reserve for contingencies in the later years of the plan (Assumption 8). The total line allocates all the PDUFA funds FDA expects to spend through FY 2002.
- Table 3 (page 26) shows the allocation of this \$224 million by expense category. About \$39 million will be spent for pay and benefits for a net of 98 additional staff (compared to \$95.2 million for 325 additional staff in the original plan). About \$87 million is planned for IT enhancements (compared to about \$98 million in the original plan). The remainder is planned for other enhancements, operating expenses, overhead, rent, and contingencies. A summary of the change in FTE's planned each year from the PDUFA additive base levels on page 5 are shown below.

PDUFA II Program FTE Changes from the PDUFA I Additive Base

Organization	1998	1999	2000	2001	2002
CDER	+23	+61	+91	+101	+101
CBER	+16	+31	+34	+37	+37
ORA		-10	-40	-40	-40
Total	+39	+82	+85	+98	+98

- Table 4 (page 26) shows the difference between the projected fee revenues and expenditures each year and the estimated PDUFA carryover balances at the beginning and end of each year. In 1999, FDA will spend about \$11 million more than it expects to

collect; in FY 2000 about \$7.5 million more. In FY's 2001 and 2002, this plan calls for expenditures of about \$6 million and \$5.5 million less, respectively, than expected collections. FDA can do this because FY 1999 began with about \$67.5 million in PDUFA carryover funds. In FY's 1999 and 2000, when FDA will spend more than it collects, the carryover balance will decrease. In FY 2001 and 2002, when FDA will spend less than it collects, the carryover balance will increase.

While these carryover balances are sizable, FDA must have sufficient carryover funds at the end of each fiscal year in order to begin the following year with no less than 2½ months of operating funds (Assumption 3). The table below compares those minimum amounts with planned carryover balances.

Minimum Carryover Balance at the End of Each Fiscal Year and Planned (\$000)

Item	1999	2000	2001	2002
Plan for Following Year	\$140,363	\$143,223	\$150,202	\$157,712
Minimum Carryover	\$31,191	\$31,827	\$33,378	\$35,047
Carryover Balance in Plan	\$56,546	\$49,044	\$55,095	\$60,584
Difference -- Minimum vs. Plan	\$25,355	\$17,217	\$21,717	\$25,537

Carryover balances at these levels assure adequate funds to begin operations each year and also provide minimal security (1) if there is a substantial shortfall of funds in any one particular year or (2) if the provisions of PDUFA necessitate terminating the program because appropriations are not available at required levels.

- Tables 5 and 6 (page 27) summarize the allocation of the total \$681 million that FDA plans to spend over the 5 years of PDUFA II (PDUFA I additive base plus increases) by component and by expense category, respectively. The last column in both tables shows the percent of total PDUFA II funds planned over the next 5 years. By component, CDER will be allocated 56 percent, CBER 20 percent, ORA 4 percent, overhead 9 percent, central accounts 4 percent, rental payments to GSA 3 percent, and contingency reserve 2 percent. By expense category, 56 percent of the total PDUFA II revenues will be dedicated to pay and benefits for staff (compared with 58 percent in the original plan), 13 percent for center/ORA operating costs, 13 percent for IT initiatives, 9 percent for overhead, 4 percent for central accounts, 3 percent for rental payments to GSA, and 2 percent for the contingency reserve.
- Table 7 (page 27) summarizes the total PDUFA FTE's planned each year, showing the number of FTE's paid from the salary and expense appropriations, the number of FTE's paid from fees and considered the PDUFA I additive base, and the number of FTE's added over the course of PDUFA II under this plan.

**FY 1999 Five-Year Plan Revision
FDA Plan Summary Tables--PDUFA II (\$000)**

Note: Numbers Are Rounded and May Not Add

Table1: PDUFA I Additive Base, and Estimated Funds Available

Item\Year	1998	1999	2000	2001	2002	TOTAL	Percent
Pay and Benefits for Centers/ORAs	\$61,366	\$65,219	\$68,480	\$71,904	\$75,499	\$342,469	75%
Base Operating Funds--Centers/ORAs	\$7,021	\$6,726	\$6,431	\$6,431	\$6,431	\$33,040	7%
Overhead	\$10,889	\$10,957	\$11,505	\$12,080	\$12,684	\$58,114	13%
Central Accounts	\$4,230	\$4,642	\$4,864	\$5,097	\$5,342	\$24,173	5%
Total--PDUFA I Additive Base	\$83,506	\$87,544	\$91,280	\$95,512	\$99,956	\$457,797	100%
Estimated Fee Receipts	\$117,122	\$122,527	\$132,934	\$149,273	\$155,691	\$677,547	
Available for Enhancements	\$33,616	\$34,984	\$41,654	\$53,761	\$55,735	\$219,750	

Table 2: Funds Planned for Enhancements--by Component

Component\Year	1998	1999	2000	2001	2002	TOTAL	Percent
CDER	\$20,100	\$27,737	\$30,532	\$27,356	\$27,707	\$133,432	60%
CBER	\$9,611	\$11,262	\$9,358	\$9,148	\$8,993	\$48,372	22%
ORA	\$903	(\$140)	(\$1,446)	(\$1,122)	(\$2,114)	(\$3,920)	-2%
Overhead	\$0	\$1,096	\$1,456	\$1,741	\$1,828	\$6,120	3%
Central Accounts	\$0	\$574	\$613	\$728	\$750	\$2,664	1%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,083	\$23,014	10%
Contingency Reserve	\$0	\$0	\$3,000	\$4,000	\$7,000	\$14,000	6%
Total	\$30,614	\$45,956	\$49,155	\$47,711	\$50,246	\$223,683	100%

Table 3: Funds Planned for Enhancements--by Expense Category

Expense Category\Year	1998	1999	2000	2001	2002	Total	Percent
Pay and Benefits for Centers/ORAs	\$2,263	\$6,521	\$8,668	\$10,362	\$10,880	\$38,693	17%
Support Costs for Personnel	\$1,943	\$2,097	\$2,279	\$2,271	\$2,072	\$10,660	5%
Process Enhancements	\$5,246	\$10,137	\$8,890	\$9,227	\$8,207	\$41,707	19%
IT	\$21,163	\$20,104	\$18,607	\$13,523	\$13,427	\$86,824	39%
Subtotal to Centers	\$30,614	\$38,859	\$38,443	\$35,382	\$34,586	\$177,884	80%
Overhead	\$0	\$1,096	\$1,456	\$1,741	\$1,828	\$6,120	3%
Central Accounts	\$0	\$574	\$613	\$728	\$750	\$2,664	1%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,083	\$23,014	10%
Contingency Reserve	\$0	\$0	\$3,000	\$4,000	\$7,000	\$14,000	6%
Total	\$30,614	\$45,956	\$49,155	\$47,711	\$50,246	\$223,683	100%

4. Difference Between Plans and Available Funds, with Year-End Carry-Over Balances

Category\Year	1998	1999	2000	2001	2002
Difference Between Plan & Available		(\$10,973)	(\$7,501)	\$6,051	\$5,489
Est. Carry-Over Balance-Year Beginning		\$67,518	\$56,546	\$49,044	\$55,095
Est. Carry-Over Balance-Year End	\$67,518	\$56,546	\$49,044	\$55,095	\$60,584

**FY 1999 Five-Year Plan Revision
FDA Plan Summary Tables--PDUFA II (\$000)**

Note: Numbers Are Rounded and May Not Add

Table 5: FDA Summary of all PDUFA Additive Resources--by Component

Component\Year	1998	1999	2000	2001	2002	TOTAL	Percent
CDER	\$64,199	\$76,031	\$81,052	\$80,215	\$83,020	\$384,517	56%
CBER	\$27,684	\$28,381	\$26,947	\$27,542	\$28,231	\$138,785	20%
ORA	\$7,118	\$6,393	\$5,355	\$5,961	\$5,265	\$30,092	4%
Overhead	\$10,889	\$12,052	\$12,961	\$13,821	\$14,512	\$64,235	9%
Central Accounts	\$4,230	\$5,216	\$5,476	\$5,825	\$6,091	\$26,838	4%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,083	\$23,014	3%
Contingency Reserve	\$0	\$0	\$3,000	\$4,000	\$7,000	\$14,000	2%
Total	\$114,120	\$133,500	\$140,435	\$143,223	\$150,202	\$681,480	100%

Table 6: FDA Summary of all PDUFA Additive Resources--by Expense Category

Expense Category\Year	1998	1999	2000	2001	2002	TOTAL	Percent
Pay and Benefits for Centers/ORA	\$63,629	\$71,741	\$77,148	\$82,266	\$86,379	\$381,163	56%
Operating Funds--Excluding IT	\$14,210	\$18,960	\$17,600	\$17,929	\$16,710	\$85,407	13%
Information Technology	\$21,163	\$20,104	\$18,607	\$13,523	\$13,427	\$86,824	13%
Overhead	\$10,889	\$12,052	\$12,961	\$13,821	\$14,512	\$64,235	9%
Central Accounts	\$4,230	\$5,216	\$5,476	\$5,825	\$6,091	\$26,838	4%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,083	\$23,014	3%
Contingency Reserve	\$0	\$0	\$3,000	\$4,000	\$7,000	\$14,000	2%
Total	\$114,120	\$133,500	\$140,435	\$143,223	\$150,202	\$681,480	100%

Table 7: FDA Summary of all PDUFA FTE's for CDER, CBER, and ORA

Expense Category\Year	1998	1999	2000	2001	2002
Base FTE's Paid from Appropriations	1,147	1,147	1,147	1,147	1,147
PDUFA I Additive Base FTE's	659	659	659	659	659
FTE's Added for PDUFA II	39	82	85	98	98
Total	\$1,845	\$1,888	\$1,891	\$1,904	\$1,904

Annual Reassessments

As initially envisioned, this plan will continue to be revised each year based on the latest information available. This plan is intended to let the centers and ORA know the amounts to expect each year. This early information should facilitate the work required to meet the PDUFA II goals. Actual workload and revenues must be monitored closely.

The plan is meant to be a dynamic framework for the investments FDA must make. It will be updated in the second quarter of each fiscal year. That update will take into account the actual accomplishments, workload, revenues, and expenses of the previous fiscal year and the planned accomplishments, workload, revenues and fees to be charged in the current year, as set out in the annual *Federal Register* fee adjustment notice.

If revenues are expected to be at levels lower than the assumptions of this plan, or if actual PDUFA expenditures by CDER, CBER or ORA in the previous year are significantly less than the amounts allocated, then cutbacks in hiring and other expenses will be required as was the case in this 1999 revision. On the other hand, if PDUFA revenues exceed planned amounts because workload increases at a rate greater than planned, the additional revenues will need to be allocated to cope with these increases. Also, if unforeseen contingencies do not necessitate using the contingency reserve, it will be allocated by the end of the second quarter of each year.

During PDUFA II, FDA's Office of Management and Systems will look closely at PDUFA costs and workload. If that assessment indicates that PDUFA workload is out of kilter with the distribution of resources in this plan, then adjustments will be made.

Because all funds FDA expects to collect have been planned, adjustments made by the centers and ORA each year will generally be within the total amounts already planned for each fiscal year. For example, if an unplanned IT item becomes a high priority, then cutbacks will have to be made in other components of that organization's plan (such as other IT items, hiring, or operating support) in order to fund that need.

PDUFA II Fee and Revenue Estimation Worksheet

Assumes 148 FAE's in 1999, and Outyear Numbers Derived From Regression Analysis

Attachment 1

		1998	1999	2000	2001	2002
Statutory Full Application Fee		\$250,704	\$256,338	\$256,338	\$267,606	\$258,451
Inflation Percentage	1	2.45%	6.22%	9.41%	12.69%	16.07%
Fee per Full Application, after Inflation		\$256,846	\$272,283	\$280,451	\$301,562	\$299,983
Estimated Equivalent of Full Applications	2	152	150	158	165	173
Est. Total Application Fee Revenue		\$39,040,592	\$40,842,395	\$44,311,276	\$49,757,802	\$51,897,083
After Accounting for Waivers						
Est. Total Product Fee Revenue		\$39,040,592	\$40,842,395	\$44,311,276	\$49,757,802	\$51,897,083
Estimated # of Products		2100	2100	2100	2100	2100
Product Fee		\$18,591	\$19,449	\$21,101	\$23,694	\$24,713
Est. Total Establishment Fee Revenue		\$39,040,592	\$40,842,395	\$44,311,276	\$49,757,802	\$51,897,083
Estimated # of Establishments		275	275	275	275	275
Establishment Fee		\$141,966	\$148,518	\$161,132	\$180,937	\$188,717
Estimate of Total Revenue		\$117,121,776	\$122,527,185	\$132,933,827	\$149,273,407	\$155,691,248
Five-Year Total:						\$677,547,444

1 Calculated at 2.45% in 1998, 3.68% in 1999, and estimated at 3% each year thereafter.

2 Number of Full Application Equivalents after allowing for Exemptions and Waivers, from Regression Analysis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Administration for Children and Families

Proposed Information Collection Activity; Comment Request

Proposed Project:

Title: Child Care and Development Fund Tribal Plan Preprint.

OMB No.: New.

Description: The Child Care and Development Fund Plan Preprint serves

as the agreement between the grantee (Indian Tribe or tribal organization) and the Federal government as to how the Block Grant programs will be operated. The plans provide assurances that the CCDF funds will be administered in conformance with legislative requirements, Federal regulations at 45 CFR parts 98 and 99 and other applicable instructions or guidelines issued by the Administration for Children and Families (ACF). The Tribal Plan Preprint (ACF Form 118A) is currently approved through 5/31/00

under the Plan Preprint approval for both State and Indian Tribes (OMB Approval Number 0970-0114). Since the tribal plan preprint must be revised to reflect the CCDF amended regulations (published 7/24/98 at 63 FR 39936-39998), it is being disaggregated from the State plan preprint approval. Therefore, a new collection and OMB control number is requested.

Respondents: State, Local or Tribal Government.

ANNUAL BURDEN ESTIMATES

Instrument	Number of respondents	Number of responses per respondent	Average burden hours per response	Total burden hours
CCDF Plan Preprint	253	.5	35	4,427
CCDF Plan Amendments	253	.5	3	380

Estimated Total Annual Burden Hours: 4,807.

In compliance with the requirements of Section 3506(c)(2)(A) the Paperwork Reduction Act of 1995, the Administration for Children and Families is soliciting public comment on the specific aspects of the information collection described above. Copies of the proposed collection of information can be obtained and comments may be forwarded by writing to the Administration for Children and Families, Office of Information Services, 370 L'Enfant Promenade, S.W., Washington, D.C. 20447, Attn: ACF Reports Clearance Officer. All requests should be identified by the title of the information collection.

The Department specifically requests comments on: (a) whether the proposed collection of information is necessary for the proper performance of the functions of the agency, including whether the information shall have practical utility; (b) the accuracy of the agency's estimate of the burden of the proposed collection of information; (c) the quality, utility, and clarity of the information to be collected; and (d) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques or other forms of information technology. Consideration will be given to comments and suggestions submitted within 60 days of this publication.

Dated: December 15, 1998.

Bob Sargis,

Acting Reports Clearance Officer.

[FR Doc. 98-33792 Filed 12-21-98; 8:45 am]

BILLING CODE 4184-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Establishment of Prescription Drug User Fee Rates for Fiscal Year 1999

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the rates for prescription drug user fees for fiscal year (FY) 1999. The Prescription Drug User Fee Act of 1992 (the PDUFA), as amended by the Food and Drug Administration Modernization Act of 1997 (the FDAMA), authorizes FDA to collect user fees for certain applications for approval of drug and biological products, on establishments where the products are made, and on such products. Fees for applications for FY 1999 were set by the FDAMA, subject to adjustment for inflation. Total application fee revenues fluctuate with the number of fee-paying applications FDA receives. Fees for establishments and products are calculated so that total revenues from each category will approximate FDA's estimate of the revenues to be derived from applications.

FOR FURTHER INFORMATION CONTACT: Michael E. Roosevelt, Office of Financial Management (HFA-120), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-5088.

SUPPLEMENTARY INFORMATION:

I. Background

The PDUFA (Pub. L. 102-571), as amended by the FDAMA (Pub. L. 105-115), establishes three different kinds of user fees. Fees are assessed on: (1) Certain types of applications and supplements for approval of drug and biological products, (2) certain establishments where such products are made, and (3) certain products (21 U.S.C. 379h(a)). When certain conditions are met, FDA may waive or reduce fees (21 U.S.C. 379h(d)).

For 1998 through 2002, under the amendments enacted in the FDAMA, the application fee rates are set in the statute, but are to be adjusted annually for cumulative inflation since 1997. Total application fee revenues are structured to increase or decrease each year as the number of fee-paying applications submitted to FDA increases or decreases (workload adjustment).

For 1998 through 2002, FDA is required to set fee rates for establishment and product categories each year, so that the total fee revenue from each of these two categories are projected to be equal to the total revenue FDA expects to collect from application fees that year. This procedure continues the arrangement under which one-third of the total user fee revenue is projected to come from each of the three types of fees-- application fees, establishment fees, and product fees.

This notice establishes fee rates for FY 1999 for application, establishment, and product fees. These fees are retroactive to October 1, 1998, and will remain in effect through September 30, 1999. For fees already paid on applications and supplements submitted on or after

October 1, 1998, FDA will bill applicants for the difference between fees paid and fees due under the new fee schedule. For applications and supplements submitted after December 31, 1998, the new fee schedule must be used. Invoices for establishment and product fees for FY 1999 will be issued in December 1999, using the new fee schedules.

II. Inflation and Workload Adjustment Process

The PDUFA, as amended by the FDAMA, provides that fee rates for each FY shall be adjusted by notice in the **Federal Register**. The adjustment must reflect the greater of: (1) The total percentage change that occurred during the preceding FY in the Consumer Price Index (CPI), or (2) the total percentage pay change for that FY for Federal employees stationed in the Washington, DC metropolitan area. The FDAMA provides for this annual adjustment to be cumulative and compounded annually after 1997 (see 21 U.S.C. 379h(c)(1)).

The FDAMA also structures the total application fee revenue to increase or decrease each year as the number of fee-paying applications submitted to FDA increases or decreases. This provision allows revenues to rise or fall as this portion of FDA's workload rises or falls. To implement this provision each year, FDA will estimate the number of fee-paying applications it anticipates receiving. The number of applications estimated will then be multiplied by the inflation-adjusted statutory application fee. This calculation will produce the FDA estimate of total application fee revenues to be received.

The PDUFA also provides that FDA shall adjust the rates for establishment and product fees so that the total revenues from each of these categories is projected to equal the revenues FDA expects to collect from application fees that year. The FDAMA provides that the new fee rates based on these calculations be adjusted within 60 days after the end of each FY (21 U.S.C. 379h(c)(2)).

III. Inflation Adjustment and Estimate of Total Application Fee Revenue

The FDAMA provides that the application fee rates set out in the statute be adjusted each year for cumulative inflation since 1997. It also provides for total application fee revenues to increase or decrease based on increases or decreases in the number of fee-paying applications submitted.

A. Inflation Adjustment to Application Fees

Application fees are assessed at different rates for qualifying applications depending on whether the applications require clinical data on safety or effectiveness (other than bioavailability or bioequivalence studies) (21 U.S.C. 379h(a)(1)(A) and (b)). Applications that require clinical data are subject to the full application fee. Applications that do not require clinical data and supplements that require clinical data are assessed one-half the fee of applications that require clinical data. If FDA refuses to file an application or supplement, 75 percent of the application fee is refunded to the applicant (21 U.S.C. 379h(a)(1)(D)).

The application fees described previously are set out in the FDAMA for 1999 (\$256,338 for applications requiring clinical data, and \$128,169 for applications not requiring clinical data or supplements requiring clinical data) (21 U.S.C. 379h(b)(1)), but must be adjusted for cumulative inflation since 1997. That adjustment each year is to be the greater of: (1) The total percentage change that occurred during the preceding FY in the CPI (all items; U.S. city average); or (2) the total percentage pay change for that FY for Federal employees, as adjusted for any locality-based payment applicable to employees stationed in the District of Columbia. The FDAMA provides for this annual adjustment to be cumulative and compounded annually after 1997 (see 21 U.S.C. 379h(c)).

The adjustment for FY 1998 was 2.45 percent (62 FR 64849, December 9, 1997). This was the greater of the CPI increase for FY 1997 (2.15 percent) and the increase in applicable Federal salaries (2.45 percent).

The adjustment for FY 1999 is 3.68 percent. This is the greater of the CPI increase for FY 1998 (1.49 percent) and the increase in applicable Federal salaries (3.68 percent).

Compounding these amounts (1.0245 times 1.0368) yields a total compounded inflation of 6.22 percent for FY 1999. The adjusted application fee rates are computed by applying the inflation percentage for FY 1999 (106.22 percent) to the FY 1999 statutory application fee rates stated previously. For FY 1999 the adjusted application fee rates are \$272,282 for applications requiring clinical data, and \$136,141 for applications not requiring clinical data or supplements requiring clinical data. These amounts must be submitted with all applications during FY 1999.

B. Estimate of Total Application Fee Revenue

Total application fee revenues for 1999 will be determined by the number of fee-paying applications FDA receives in FY 1999 (from October 1, 1998, through September 30, 1999) multiplied by the fee rates calculated in the preceding paragraph. Before fees can be set for establishment and product fee categories, each of which are projected to be equal to total revenues FDA collects from application fees, FDA must first estimate its total 1999 application fee revenues. To do this FDA has traditionally calculated the number of full application fees FDA received in the preceding fiscal year, made an allowance for waivers and exemptions, and used that figure as a basis for estimating the next year's application volume.

For FY 1998, FDA received and filed 101 human drug applications that require clinical data for approval, 23 that did not require clinical data for approval, and 93 supplements to human drug applications that require clinical data for approval. Because applications that do not require clinical data and supplements that require clinical data are assessed only one-half the full fee, the equivalent number of these applications subject to the full fee is determined by summing these categories and dividing by 2. This amount is then added to the number of applications that require clinical data to arrive at the equivalent number of applications that may be subject to full application fees.

In addition, as of September 30, 1998, FDA assessed fees for three applications that required clinical data, one application that did not require clinical data, and one supplement, all of which were refused filing or withdrawn before filing. After refunds, the full application paid one-fourth the full application fee and is counted as one-fourth of an application, and the application that did not require clinical data and the supplement each paid one-eighth of the full application fee and are each counted as one-eighth of an application.

Using this methodology, the approximate equivalent number of applications that required clinical data and were subject to fees in FY 1998 was 160, before any exemptions, waivers or reductions. Under the FDAMA, FDA may waive fees for certain small businesses submitting their first application and certain orphan products are exempted from application fees. In addition, the FDAMA excludes from fees bulk biological products that are further manufactured, and provides

exceptions for certain supplements for pediatric indications. In FY 1998 waivers or exemptions applied to 41.5 equivalents of full applications. Therefore, based solely on 1998 data, FDA estimates that approximately 118.5 (160 minus 41.5) equivalent

applications that require clinical data will qualify for fees in FY 1999, after allowing for exemptions, waivers, or reductions.

This estimate based on the data from 1998 alone predicts a substantial drop in applications, and represents a

substantial departure from FDA experience over the past 5 years. Over that period the estimated number of fee-paying applications increased fairly consistently at a rate of about 7 percent each year, as set out in Table 1 of this document.

TABLE 1.

Year	Estimated Number of Fee-Paying Full Application Equivalents
1993	116
1994	124
1995	131
1996	141
1997	169
1998	118.5

Since the volume of fee-paying applications FDA received in 1998 represents such a substantial departure from the trend experienced over the previous 5 years, and since sharp changes produce disruptive volatility in both fees and revenues, FDA reexamined the process to be used in estimating the next year's application volume. FDA considered several different approaches (continuation of current method, using a 2- or 3-year rolling average, and linear regression) and chose the linear regression projection method as the best alternative for this estimate.

Linear regression is well suited to situations like this where there are several years of historical data, the potential exists for shifts from year-to-year, and there is no obvious causative rationale to reasonably predict the year-to-year fluctuations. It also provides a

damping effect on year-to-year fee and revenue fluctuations and allows for more stability in both fee levels paid by industry and in agency resource planning. Under this approach, the analysis takes into account the number of fee-paying PDUFA submissions each year since PDUFA began in 1993, adjusts those numbers conservatively to reflect additional exemptions/waivers that would have been granted between 1993 and 1997 if the current law governing exemptions and waivers had been in effect then, and fits the best line to those data points. The extension of that line to the next year estimates the number of submissions for that year. Beginning now for FY 1999, FDA will make this annual estimate based on a linear regression analysis of data on all fee-paying full application equivalent submissions from 1993 through the latest year (1998 in this case).

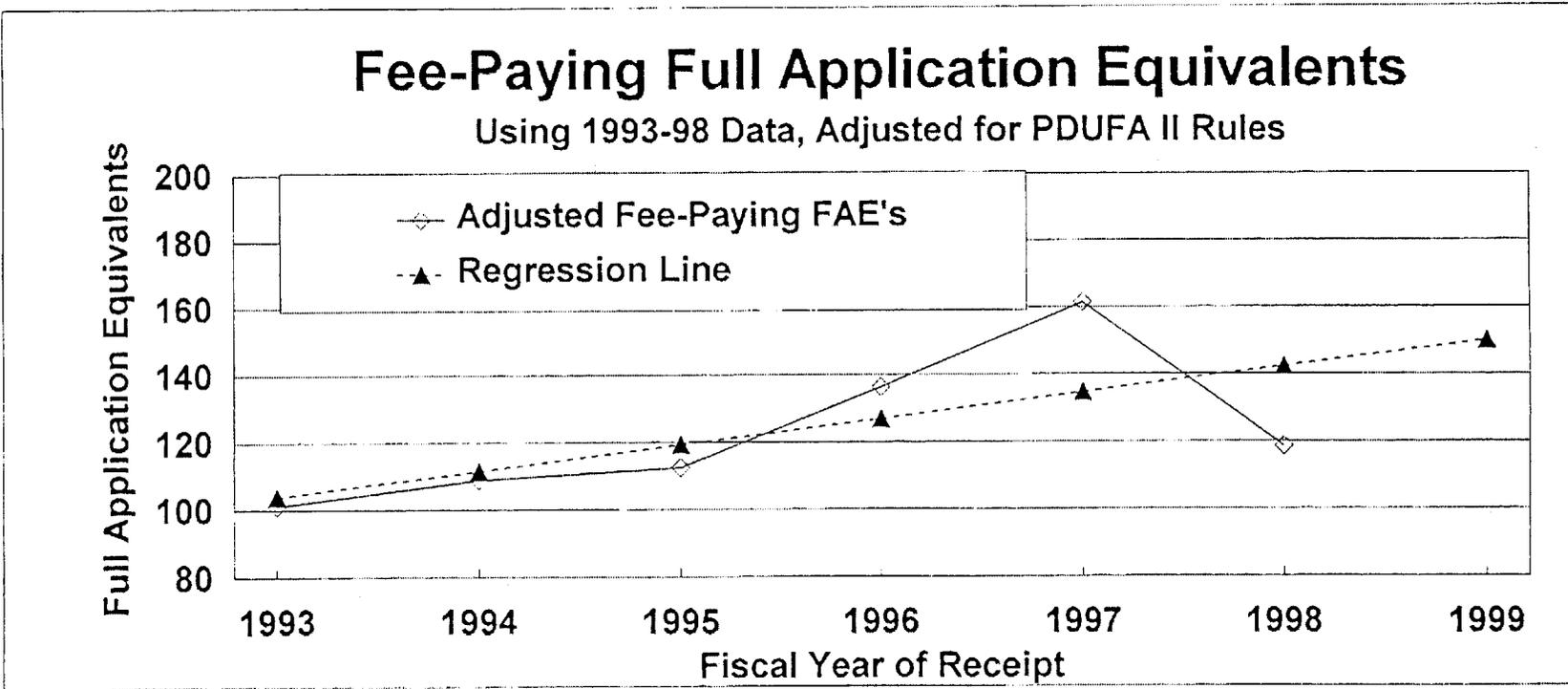
This will mean that our estimated number of applications will be higher in 1998 than it would have been under our previous estimating method. It will also mean that in future years, if there is a sudden rise in application volume, the regression analysis process will dampen the effect of such year-to-year increases as well. We believe that this is a fair and reasonable approach, and that it will insulate fees and revenues from significant fluctuations that may occur in any single year.

Using this approach, a linear regression line based on the adjusted number of fee-paying full application equivalent submissions since 1993 projects the receipt of 150 fee-paying full application equivalent submissions in 1999, as reflected in Table 2 and the graphic of this document.

TABLE 2.

Year	1993	1994	1995	1996	1997	1998	1999
Adjusted Fee-Paying Full Application Equivalents	101.0	108.9	112.5	136.3	161.5	118.5	
Regression Line	103.9	111.6	119.3	127.0	134.6	142.3	150.0

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The total FY 1999 application fee revenue is estimated by multiplying the adjusted application fee rate (\$272,282) by the equivalent number of applications projected to qualify for fees in FY 1999 (150), for a total estimated application fee revenue in 1999 of \$40,842,300. This is the amount of revenue that FDA is also expected to derive both from establishment fees and from product fees.

IV. Fee Calculations for Establishment and Product Fees

A. Establishment Fees

At the beginning of FY 1998 the establishment fee was based on an estimate of 275 establishments subject to fees. By the end of FY 1998, 343 establishments qualified for and were

billed for establishment fees, before all decisions on requests for waivers or reductions were made. We estimate that a total of 25 establishment fee waivers will be granted in 1998, for a net of 318 fee-paying establishments. In FY 1999 fees will be based on an estimate of 318 establishments paying fees after taking waivers into account. The fee per establishment is determined by dividing the adjusted total fee revenue to be derived from establishments (\$40,842,300), by the estimated 318 establishments, for an establishment fee rate for FY 1999 of \$128,435 (rounded to the nearest dollar).

B. Product Fees

At the beginning of FY 1998 the product fee was based on an estimate that 2,100 products would be subject to

product fees. By the end of FY 1998, 2,279 products qualified and were billed for product fees before all decisions on requests for waivers or reductions were made. Assuming that there will be about 55 waivers granted, FDA estimates that 2,224 products will qualify for product fees in FY 1999, after allowing for waivers and exemptions. Accordingly, the FY 1999 product fee rate is determined by dividing the adjusted total fee revenue to be derived from product fees (\$40,842,300) by the estimated 2,224 products for a product fee rate of \$18,364 (rounded to the nearest dollar).

V. Adjusted Fee Schedules for FY 1999

The fee rates for FY 1999 are set out in Table 3 of this document.

TABLE 3.

Fee Category	Fee Rates For FY 1999
Applications	
Requiring clinical data	\$272,282
Not requiring clinical data	\$136,141
Supplements requiring clinical data	\$136,141
Establishments	\$128,435
Products	\$18,364

VI. Implementation of Adjusted Fee Schedule

A. Application Fees

Any application or supplement subject to fees under the PDUFA that is submitted after December 31, 1998, must be accompanied by the appropriate application fee established in the new fee schedule. Payment must be made in United States currency by check, bank draft, or U.S. postal money order payable to the order of the U.S. Food and Drug Administration. Please include the user fee ID number on your check.

Your check can be mailed to: Food and Drug Administration, P.O. Box 360909, Pittsburgh, PA 15251-6909.

If checks are to be sent by a courier that requests a street address, they can be sent to: Mellon Bank, Three Mellon Bank Center, 27th Floor (FDA 360909), Pittsburgh, PA 15259-0001. (Note: This Mellon Bank Address is for courier delivery only.) Please make sure that the FDA P.O. Box number (P.O. Box 360909) is on the enclosed check.

FDA will bill applicants who submitted application fees between October 1, 1998, and December 31, 1998, based on the adjusted rate schedule.

B. Establishment and Product Fees

By December 31, 1998, FDA will issue invoices for establishments and product fees for FY 1999 under the new fee schedules. Payment will be due by January 31, 1999. FDA will issue invoices in October 1999 for any products and establishments subject to fees for FY 1999 that qualify for fees after the December 1998 billing.

Dated: December 15, 1998.

William K. Hubbard,
Associate Commissioner for Policy
Coordination.

[FR Doc. 98-33831 Filed 12-21-98; 8:45 am]
BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Indian Health Service

List of Recipients of Indian Health Scholarship Under the Indian Health Scholarship Program

The regulations governing Indian Health Care Improvement Act Programs (Pub. L. 94-437) provide a 42 CFR 36.334 that the Indian Health Service shall publish annually in the *Federal Register* a list of recipients of Indian Health Scholarships, including the name of each recipient, school and

tribal affiliation, if applicable. These scholarships were awarded under the authority of Section 103 and 104 of the Indian Health Care Improvement Act, 25 U.S.C. 1613-1613a, as amended by the Indian Health Care Amendments of 1988, Pub. L. 100-713.

The following is a list of Indian Health Professions Scholarship Recipients for Fiscal Year 1998:

- Ables, Millicent Elaine, University of Kansas, Choctaw Nation of Oklahoma
- Abold-Arellano, Carol Ann, University of South Dakota, Oglala Sioux of the Pine Ridge Reservation
- Adair, Roger Willard, Arizona State University, Cherokee Nation of Oklahoma
- Adams, Hayley M., University of Alaska/Anchorage, Nenana Native Association, AK
- Aguilar, Dolores E., Presentation College, Cheyenne River Sioux Tribe
- Akers, Margaret Ann, University of Tulsa, Muskogee (Creek) Nation, Oklahoma
- Albert, Corrina D., University of New Mexico, Pueblo of Laguna
- Alexander, Andrea Lynn, Oklahoma State University, Seminole Nation of Oklahoma
- Alexander, Lisa Kalliah, University of Washington School of Med., Confederated Tribes of the Grand Ronde
- Allery, Crystal Vernelle, Minot State University, Turtle Mountain Band Chippewa
- Allick, Albert P., University of Minnesota Duluth Med School, Turtle Mountain Band of Chippewa
- Allison, Rochelle Jade, University of New Mexico, Navajo Tribe of AZ, NM, & UT

**PRESCRIPTION DRUG USER FEE ACT
(PDUFA II) INFORMATION MANAGEMENT
FIVE YEAR PLAN**

FY 1999 Revision

July 1999

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Appendix A: ERSR Program Budget
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1.0 BACKGROUND

The Prescription Drug User Fee Act of 1992 (PDUFA) provided FDA with increasing levels of resources for the review of human drug applications. That Act expired on September 30, 1997, but the FDA Modernization Act (FDAMA) of 1997 amended PDUFA and extended it through September 30, 2002 (PDUFA II). This extension will enable FDA to accomplish increasingly challenging goals over the next five years. PDUFA, as amended and extended by FDAMA, and with its new goals, is referred to as PDUFA II and its predecessor is now referred to as PDUFA I.

PDUFA II commits FDA to substantially faster review of some applications, to new goals for responding to industry requests for meetings and documenting outcomes of those meetings and for handling dispute resolutions, and to the transition to electronic receipt and review of applications by 2002. The new goals of PDUFA II are challenging, diverse, and resource intensive. Major components of the review process will be accelerated further. Many of the goals will require the development of technology standards and issuance of guidance documents. The development of infrastructure to provide the tools necessary to move to electronic application receipt and review also will be essential.

The Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Office of Regulatory Affairs (ORA) have collaborated with the Chief Information Officer and the Office of Information Resources Management (OIRM) to develop an Agency-wide Information Management plan for investing PDUFA II information technology (IT) dollars in an Electronic Regulatory Submission and Review (ERSR) Program. This program and its component projects will support the transition from a largely paper-based regulatory submission and review environment to an electronic environment.

In 1998, the Agency published a PDUFA II Information Management Five-Year Plan that described the strategy for budgeting, managing and expending PDUFA II IT funds during the period FY 1998 to FY 2002. That initial document provided a conceptual view of the components within the ERSR Program. It described the purpose and activities within the PDUFA II ERSR Program, provided a milestone schedule for executing that program, and explained the procedures and policies for monitoring the progress of the program.

1.1 Purpose of this Document

This document provides an update to the planned activities within the ERSR Program. Over the past year, the details and design specifications for several components evolved as Centers refined their respective IT projects to better fit under the ERSR umbrella and to conform to FDAMA mandates. Additionally, revenue forecasts have declined as explained in the PDUFA II Five-Year Plan (1999 Revision). This document provides a project-oriented view of the ERSR program under these new conditions and presents 1) how projects support accomplishing the overall ERSR goal, 2) insight to near-term and ultimate project milestones, and 3) budgets for the ERSR projects.

This document is intended to be a "living" document that guides oversight of the expenditure of PDUFA II IT funds. The document is revisited annually to refine scheduling and budgeting forecasts, factor in actual expenses of previous years, and incorporate additional projects as they are identified.

1.2 Document Organization

The 1999 PDUFA II Information Management Five-Year Plan (FY 1999 Revision) is organized as follows:

- Section 2.0 describes the PDUFA II goals supported by the establishment and implementation of the ERSR Program. It also describes the underlying Agency IT goals and objectives driving the ERSR Program within the Agency's integrated systems architecture and common computing environment;
- Section 3.0 provides an overview of the PDUFA II ERSR Program and describes the strategy for meeting the program goals;
- Section 4.0 presents the projects within the ERSR Program, maps those projects to their respective ERSR subgoals, and presents milestones for project activities;
- Section 5.0 summarizes the overall plan for implementing the ERSR program; and
- Section 6.0 presents the overall mechanisms in place to monitor the progress of the ERSR program.

ERSR Program costs are provided in Appendix A. A list of acronyms is provided as Appendix B.

2.0 PDUFA II GOALS

The Agency's PDUFA II program provides funding to implement information technology initiatives that support the expedited approval of human drugs and biological products. PDUFA II goals require the Agency's transition from a largely paper-based regulatory submission and review environment to a new electronic paperless submission and review environment.

New performance goals require even faster review times than the goals established and achieved with the original PDUFA legislation. These goals involve further accelerating over five years (FY 1998 through FY 2002) the review of submissions such as New Drug Applications (NDAs), Product License Applications (PLAs), Biologic License Applications (BLAs), efficacy supplements, and manufacturing supplements. Additionally, PDUFA II identified other performance goals in new areas such as responding to industry requests for meetings, providing industry with meeting minutes, and resolving disputes.

From an Information Technology perspective, however, the primary PDUFA performance goal states:

"The Agency shall develop and update its information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs and human drug applications, as defined in PDUFA, and related submissions."

FDA defines "paperless" as an environment with the requisite systems that will provide the capability and capacity for the receipt, review, and tracking of electronic submissions. While PDUFA II specifies INDs and human drug applications, CBER and CDER are planning to accommodate more than those submissions in their environments.

The ERSR Program, therefore, represents the Agency's activities to transition to an environment that will accommodate paperless receipt and processing of submissions. This transition requires the Agency to fulfill four high-level objectives or subgoals:

- Establish standards for the format, content, and technical specifications for electronic submissions;
- Provide guidance for industry to follow in preparing electronic submissions;
- Design and implement systems to provide the capability and capacity for the receipt, review, and tracking of electronic submissions; and
- Update the technical and non-technical infrastructure to support an electronic review environment.

Within the ERSR Program, activities to meet PDUFA II goals are augmented by Agency-wide efforts to meet IT goals established by the Agency's CIO. The CIO oversees the Agency's IT efforts to meet the challenge to maintain an aggressive application of new technology through an Agency-wide approach to investment selection and decision-making. Balance must be achieved between an increasing workload, unique organizational business needs, and technology and information integration across the Agency. This balance requires review of Agency IT investments by FDA executive leadership, a sound technology base upon which these applications will reside, and a viable set of Agency IT goals. To meet this challenge, the FDA is establishing an IT program to manage resources Agency-wide with the following goals:

- Facilitate information sharing within FDA by creating a common computing environment across the Agency;
- Reduce the regulatory burden on U.S. industry and the economy through the implementation of effective IT;
- Facilitate the development of innovative technology solutions that support the regulatory process and improve the timely availability and ensure the safety of regulated products;

- Upgrade the FDA's ability to disseminate information to the public, academia, the scientific community, and industry through the evolution and sustainment of an integrated information environment throughout the Agency; and
- Create and sustain an effective IT Investment Review Process.

To ensure that the ERSR Program conforms to the overall FDA IT Program, the following objectives were developed:

- Transition to a paperless, or near paperless, environment for program and administrative processes;
- Elimination of redundant or duplicate processes wherever feasible;
- Seamless, fast exchange of information within and across Centers and external to the Agency;
- Rigorous records management and document control, tracking, archiving;
- Robust electronic data interchange (EDI) capability for business and program data exchange;
- Standards-based information technology infrastructure; and
- Standards-based information repositories and data dictionaries.

The PDUFA II ERSR Program has afforded the Agency's PDUFA-funded organizations the opportunity to continue transitioning from a largely paper-based paradigm to a paperless environment well in advance of the requirements of the Government Paperwork Elimination Act (GPEA). GPEA guidance requires Federal agencies to give persons who are required to maintain, submit, or disclose information the option of doing so electronically when practicable as a substitute for paper, and to use electronic authentication methods to verify the identity of the sender and integrity of the document. In their efforts to comply with GPEA, other FDA organizations will benefit significantly from the technological advances made in the PDUFA organizations through the ERSR Program.

The following section presents the overall strategy for transitioning to a computing environment that will accommodate paperless receipt and processing of submissions.

3.0 ELECTRONIC REGULATORY SUBMISSION AND REVIEW (ERSR) PROGRAM STRATEGY

As mentioned in the previous section, the ERSR Program supports the transition from a largely paper-based regulatory submission and review environment to an electronic environment. The ERSR Program is comprised of a variety of projects, each of which is designed to satisfy a different part of the primary PDUFA IT goal. Additionally, various organizations are responsible for the successful implementation of the ERSR Program.

Roles and Responsibilities

The principal organizations benefiting from user fees are the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER). These organizations ultimately are responsible for establishing the capability and capacity to receive, process, and archive submissions electronically within their organizations. These Centers are responsible for addressing the needs of the Agency's Office of Regulatory Affairs (ORA) in accessing information necessary to conduct field inspection activities. ORA, in turn, is responsible for ensuring their field offices have the infrastructure needed to interface with CDER and CBER electronically where necessary. Finally, the Chief Information Officer (CIO) and the Office of Information Resources Management (OIRM) are responsible for ensuring that all PDUFA II IT investments support the Agency's common IT goals, fit into a common computing environment, and follow good IT management practices.

Approach

CDER and CBER's responsibilities in performing product safety and efficacy review activities are similar. However, the products for which CBER and CDER are responsible are very different. The differences in review requirements for handling these products are founded on both legislative and scientific bases. Both organizations are governed by different regulatory statutes and mandates that require different approaches to their respective review processes. Consequently, over time, CBER and CDER's organizational structures have evolved to the business rules and supporting processes specific to their mission and product requirements. For example, CDER's Office of Review Management is organized according to scientific discipline (e.g., Neuropharmacological, Cardio-Renal, Oncologic) and each NDA is addressed by each of the scientific discipline offices during the product review. CBER, however, is organized by product (e.g., Blood, Vaccines, Therapeutics) and the majority of the review is handled within the respective product office.

While internal business processes have evolved based on organizational culture and Center-specific re-engineering efforts, these rules and processes have been harmonized where there were similarities in functions and where there were cost efficiencies to be gained. An overarching goal of ERSR is to create a transparent interface between Industry and the Agency. To this end, CBER and CDER are collaborating to develop common technology standards and information formats for electronic submissions. These standards are intended to enable Industry to prepare "modular" submissions that can be sent to either Agency organization without significant reformatting.

The ERSR Program has been shared widely with industry since the mid-1990s via conferences and workshops sponsored by the Drug Information Association (DIA), collaboration with PhRMA's Regulatory Affairs Committee (RAC) and RAC's Electronic Regulatory Submissions (ERS) Working Group, participation in the International Conference on Harmonization (ICH) expert working groups, and presentations at industry trade meetings. Through this extensive collaboration within the Agency and with external parties, and as a result of subsequent voluntary pilots with regulated firms, the electronic submission of Case Report Tabulations (CRTs) and Case Report Forms (CRFs) in Portable Data Format

(PDF) was implemented without major problems¹. This early accomplishment under the ERSR Program demonstrates a successful partnership between the Agency and the industry it regulates. This partnership represents the type of mutual cooperation between FDA and Industry that will be key to achieving a paperless review by FY 2002.

Figure 1 provides a conceptual view of the ERSR Program. The explanation following Figure 1 presents the dependencies of the various portions of the Program and shows how they support the ERSR subgoals.

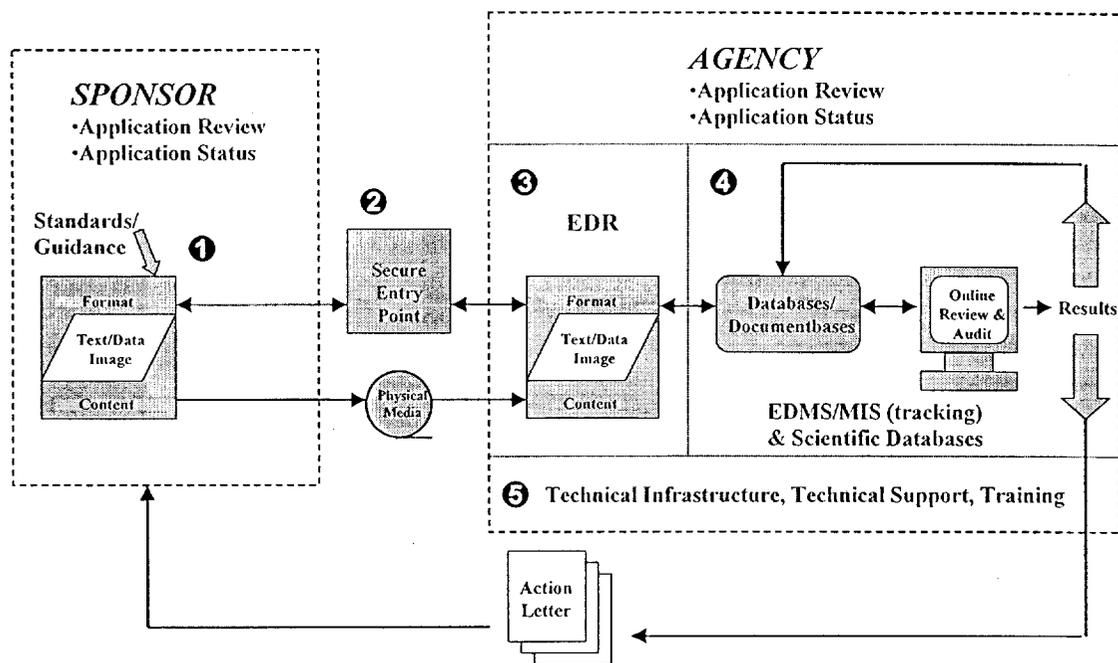


Figure 1

Establish standards (1)

FDA participates in several standards-related projects to define the format and content of regulatory submissions. The Agency actively participates in activities of the International Conference on Harmonization (ICH), which is a science-driven initiative to curtail regulatory duplication by working towards a common worldwide drug and biologic registration package. These standards activities are essential for ensuring a consistent basis upon which to provide guidance to industry for electronic submissions. Additionally, the Agency must establish and implement standards for secure messaging and secure communications among its Centers, other regulatory authorities, and the regulated industry.

Provide guidance and secure entry (1, 2)

Upon establishment of the standards, FDA provides written guidance for industry to follow in preparing electronic submissions. Guidance documents are posted in FDA's public docket. Industry training is provided at technical workshops and IT conferences hosted by organizations such as DIA. The development and completion of guidance documents serve as the foundation for enabling regulated industry to exchange electronic submissions with the Agency.

¹ CRTs and CRFs are paper-intensive portions of a new drug application. These parts often make up approximately two-thirds of the paper submitted with NDAs.

Electronic submissions that conform to the established standards and guidelines will be submitted via acceptable physical media or transmitted via an electronic Gateway. Electronic communication between organizations within the Agency and with external organizations will be safeguarded by means of a future Agency secure electronic messaging capability and the Agency's network firewall.

Design and implement systems (④,④)

There are various systems required to provide the capability and capacity for receiving, reviewing, and tracking submissions electronically. An electronic document room accommodates the program area receipt, archive, and storage of these submissions. Management information systems enable reviewers and field inspectors to operate in an electronic review environment with appropriate access to IND/BLA/NDA tracking data, electronic submissions, and related historical review documents and access to scientific databases and tools (SAS Transport, statistical packages, Library Electronic Reference Network (LERN)). Electronic document management systems provide capability to store, route, and retrieve at a later date resulting review documents.

Update the technical and non-technical infrastructure (⑥)

All aspects of the ERSR Program are supported by an infrastructure including standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) and additional capabilities as needed, such as future implementation of a secure e-mail package for communicating with regulated industry, capability for field component review and inspection access, and access to analytical tools needed by reviewers for use with structured databases. In addition, there are foundational support aspects to ERSR such as underlying technical architecture, training, and technical support.

The next section presents a mapping of each project within the ERSR Program to its respective ERSR subgoal and presents near-term and long-term activities associated with those projects.

4.0 IMPLEMENTATION OF THE ERSR PROGRAM

The scope of the ERSR Program is very large and encompasses a broad range of activities. To accommodate the paperless receipt and processing of submissions, the Agency must plan, coordinate, and execute activities across the ERSR Program in such a way that these actions are integrated successfully and ultimately enable the Agency to meet the overall “paperless by 2002” goal as described in Section 2.0.

The various activities within the ERSR Program have been subdivided into the four subgoals of the ERSR Program presented in Section 2.0. This section provides a description of the activities being conducted toward meeting each subgoal and a summary of milestones for those activities.

4.1 Establish Standards

ERSR Subgoal: Establish standards for the format, content, and technical specifications for electronic submissions.

The success of ERSR is dependent upon accurate and thorough definition of data and reporting standards for the format and content of regulatory submissions and the dissemination of guidance for industry to prepare submissions. Additionally, the key to success of the ERSR Program is the consistent and standard application of IT across the various systems developed and infrastructure established within the PDUFA funded organizations.

Standards for Electronic Submissions

FDA is involved in several standards-related projects that impact the definition of format and content of regulatory submissions. FDA plays an active role in the development of standards and guidelines as issued by organizations such as the National Institute of Standards and Technology (NIST), the International Organization for Standardization (ISO), and the US Pharmacopeia. Standards used and required by the Agency are consistent with the guidelines established by those organizations.

A major standards development activity in which the Agency actively participates is the International Conference on Harmonization (ICH), a collaborative effort involving the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in those three regions. The purpose of ICH is to recommend ways to achieve greater harmonization in the interpretation and application of technical guidelines and requirements to curtail regulatory duplication by working towards a common worldwide drug and biologic registration package. FDA is active in the ICH M4 Expert Working Group (EWG) that focuses on the Common Technical Document (CTD) for the technical content of sections of the NDA.

The activities within the ERSR program are influenced most by the M2 EWG of the ICH which focuses on Electronic Standards for Transmission of Regulatory Information. The goal of M2 is to identify, evaluate, and recommend appropriate and relevant standards to facilitate the electronic transfer of regulatory information between industry authorities and among regulatory agencies. The FDA representative from CDER serves as the Rapporteur for the M2 EWG and the FDA’s representative from CBER is a participant. The M2 EWG is developing a series of recommendations for facilitating electronic communications. The EWG is recommending standards for physical media, networking, secure EDI transmission over the Internet, and electronic document format. To every extent possible, FDA adheres to the standards recommended by the ICH in developing standards and guidance documents.

Throughout the remainder of the PDUFA II period, both CBER and CDER will continue to play active roles in the standards development activities of the ICH and other standards organizations and these standards will be implemented, where appropriate, within the ERSR Program.

Standard Computing Environment

Over the last few years, the Agency has been proceeding aggressively with its Information Systems Architecture (ISA) initiative. FDA has established a common computing environment through the implementation of ISA by standardizing desktops and networks across the Agency. Patchwork initiatives over time left an FDA IT environment that consisted of numerous layered and often incompatible product suites. Operating within that environment, significant time and energy were expended in moving information throughout the Agency, to the industry it regulates, and to the general population that it serves.

The IT infrastructure that the Agency is migrating toward through the ISA initiative:

- Improves communication;
- Enables collaboration;
- Increases productivity; and
- Creates a more manageable and cost effective environment.

The ISA initiative will standardize the information systems architecture of the entire Agency beginning with the e-mail system, the network operating system, and the desktop operating system. Adopting a standardized IT infrastructure, such as ISA provides many benefits to the FDA. It will accommodate IT environment improvements to optimize technology, and the FDA Baseline Infrastructure also will enable Agency collaboration and introduce dramatic productivity gains. It will improve the process of moving information throughout the Agency, to the industry it regulates and to the general population it serves, decrease operations and maintenance costs, and decrease training time and costs by providing users with system applications with a common interface.

4.2 Provide Guidance

ERSR Subgoal: Provide guidance for industry to follow in preparing electronic submissions.

Upon establishment of a common set of standards for basic document formatting, electronic integration, and electronic filings, FDA provides written guidance for industry to follow in preparing electronic submissions. Guidance documents are posted in FDA's public docket. Industry training is provided at technical workshops and IT conferences hosted by organizations such as DIA.

CBER and CDER are working collaboratively to develop a series of guidance documents to assist applicants in making regulatory submissions in electronic format. In some cases, guidance differs from CBER to CDER because of differences in the business processes and regulatory mandates between the Centers. The Centers are working to minimize differences wherever possible.

An important challenge affecting guidance for and the receipt and archive of submission is the electronic records/electronic signature issue. The final rule in the Code of Federal Regulations for electronic records/electronic signature (21 CFR Part 11) was posted in the Federal Register in March 1997. That rule explains the regulations that provide criteria for acceptance by FDA of electronic records, electronic signatures, and handwritten signatures executed to electronic records as equivalent to paper records and handwritten signatures executed on paper. The Agency plans during the ERSR Program five-year span to issue guidance to industry on the implementation of Part 11.²

Guidance documents and target dates for publishing those documents are provided below:

September 1997	(CDER) Issue guidance for archiving submissions in electronic format – NDAs. Guidance allows electronic submissions to be received in CDER without an accompanying paper copy and covers only electronic CRFs and CRTs.
April 1998	(CDER) Issue draft guidance for providing Regulatory Submissions in Electronic Format – NDAs. This guidance expands the September 1997 guidance by providing guidance on submitting a complete archive copy of the NDA in electronic format.
January 1999	(CDER) Publish final guidance for providing regulatory submissions in electronic format – NDAs.
June 1998	(CBER) Publish guidance for electronic submission of Case Report Forms (CRFs), Case Report Tabulations (CRTs) and Data to CBER.
June 1998	(CBER) Publish information regarding a pilot program for Electronic Investigational New Drug (eIND) Applications for Biological Products
June 1998	(CBER) Publish instructions for submitting electronic Lot Release Protocols to CBER.

² As the specifics for implementing Part 11 have not been determined, the impact of the rule on the technology being applied and the systems being developed within the ERSR Program will be determined and addressed as needed.

June 1998	(CBER) Publish guidance for electronic submission of a Biologics License Application (BLA), Product License Application (PLA)/Establishment License Application (ELA) to CBER
January 1999	(CDER and CBER) Publish joint guidance document on general considerations for electronic submissions.
FY 2000	FDA representatives to the ICH will be working with the organization to reach consensus on the Common Technical Document. The ICH M4 EWG is nearing consensus on harmonizing the table of contents as well as the content of clinical and non-clinical summaries and tabulations. Work has begun on making the Common Technical Document suitable for electronic submission.
June 2000	(CBER) Develop and publish guidance to define secure electronic mail general considerations for submissions.
October 2001	(CBER) Develop and issue guidance to Industry that defines electronic submission guidelines for Lot Release Protocols, Biologics License Applications, New Drug Applications, and PMAs/510Ks.
September 2002	(CDER) Develop and publish guidance documents for the electronic submission standards for text, image, and data of Investigational New Drug (IND) Applications, Drug Master Files (DMFs), and Annual Reports.

The following chart shows the schedule for these guidance activities.

PDUFA II Information Management Five-Year Plan (FY 1999 Revision)
 July 1999

Task Name	Finish	1998				1999				2000				2001				2002					
		Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	
CDER Guidance Activities	Sun 9/1/02																						
Guidance for Archiving submissions in electronic format - NDAs (CRTs/CRFs only)	Mon 9/1/97	◆ 9/1																					
Draft Guidance for Providing Regulatory submissions in electronic format - NDAs (complete archive copy)	Wed 4/1/98		◆ 4/1																				
Final guidance for providing regulatory submission in electronic format (full NDA)	Fri 1/1/99				◆ 1/1																		
Joint Guidance on general considerations for submitting applications	Fri 1/1/99				◆ 1/1																		
Continue working with ICH to reach consensus on the Common Technical Document	Thu 9/30/99									9/30													
Guidance for the electronic submission of INDs	Sun 9/1/02																						◆ 9/1
Guidance for electronic submission of Drug Master Files (DMFs)	Sun 9/1/02																						◆ 9/1
Guidance for electronic submission of Annual Reports	Sun 9/1/02																						◆ 9/1
CBER Guidance Activities	Mon 10/1/01																						
Guidance for electronic submissions of a BLA, PLA, ELA	Mon 6/1/98			◆ 6/1																			
Guidance for Electronic Submissions of CRFs, CRTs, and Data	Mon 6/1/98			◆ 6/1																			
Pilot Program for Electronic Investigational New Drug (eIND) Applications for Biological Products	Mon 6/1/98			◆ 6/1																			
Instructions for submitting electronic lot release protocols	Mon 6/1/98			◆ 6/1																			
Joint Guidance for General Considerations for Submitting Applications	Fri 1/1/99						◆ 1/1																
Continue working with ICH to reach consensus on the Common Technical Document	Thu 9/30/99											9/30											
Guidance for secure electronic mail and general considerations for submissions	Thu 6/1/00														◆ 6/1								
Guidance for submitting Lot Release Protocols electronically	Mon 10/1/01																						◆ 10/1
Guidance for submitting NDAs electronically	Mon 10/1/01																						◆ 10/1
Guidance for submitting PMAs/510Ks electronically	Mon 10/1/01																						◆ 10/1

4.3 Design and Implement Systems

ERSR Subgoal: Design and implement systems to provide the capability and capacity for the receipt, review, and tracking of electronic submissions.

The largest component of the PDUFA II ERSR Program involves the design, development, and implementation of systems that will enable the Agency to receive, review, and track submissions electronically. Electronic submissions that conform to the established standards and guidelines will be transmitted via acceptable physical media to an Electronic Document Room. Systems are being developed to provide an automated means for creating, managing, and archiving internally generated review documents. Other systems are being built to track the status and progress of submissions submitted to the Agency for action, generating mandatory user fee reports, and enabling tracking of milestones and workload statistics for improved management accountability. In addition, scientific databases, which include structured databases, reference guides, and analytical tools needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop, are an important component of the electronic submission area.

Figure 2 uses the conceptual diagram provided in Figure 1 to identify (in **SHADED BOXES**) the systems being developed within the ERSR Program. Following Figure 2 is a description of each of the systems and future activities planned for each system.

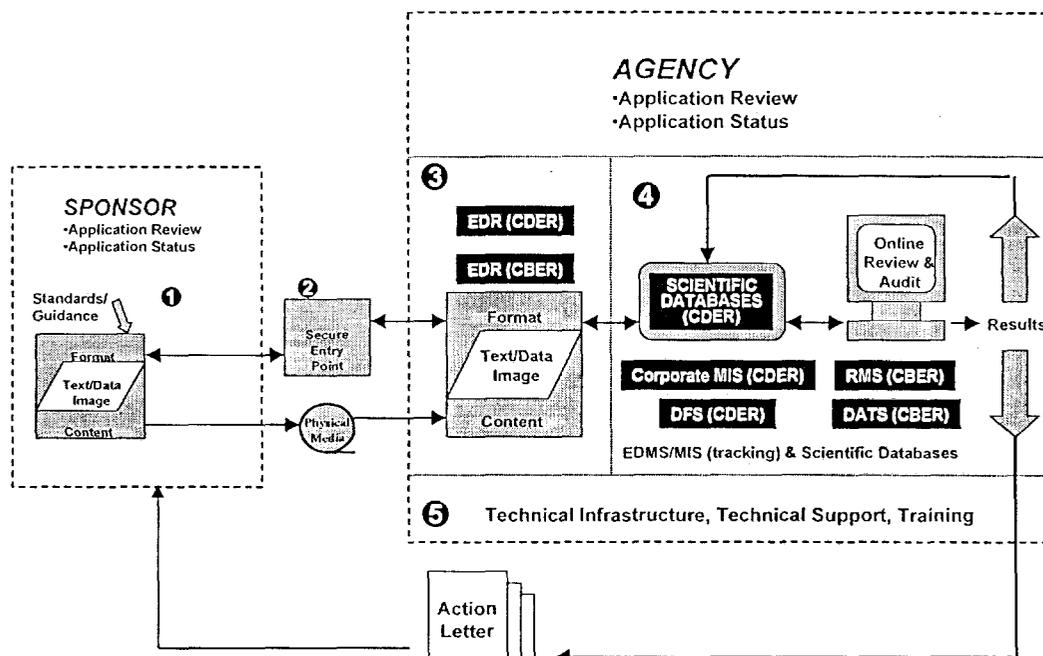


Figure 2

CDER Electronic Document Room (EDR)

CDER currently provides a capability to accommodate receipt and archive of electronic submissions. Ultimately, CDER's EDR will support receipt and archive of full New Drug Applications (NDAs), Investigational New Drugs (INDs), Drug Master Files (DMFs), and Annual Reports. Submissions to the EDR come in on one of several physical media types as defined in the industry guidance posted in the public docket.

CDER began developing its Electronic Document Room during FY 1997. The EDR was established initially to accommodate the receipt, archive, and storage of electronic Case Report Forms (CRFs) and Case Report Tabulations (CRTs) for New Drug Applications (NDAs). CDER has published Industry Guidance for submitting CRFs and CRTs without an accompanying paper copy. These CRFs and CRTs are being received in the EDR as text images in PDF for archive.

CDER's targeted activities are the following:

4 th quarter FY 1999	CDER expects to provide the capability and capacity to accommodate full electronic NDAs by September 1999.
4 th quarter FY 2001	CDER expects to have expanded the capability and capacity to accommodate INDs, DMFs, and Annual Reports by September 2001.

CDER Scientific Databases

Scientific Databases include structured databases, reference guides, and analytical tools needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop. CDER is developing carcinogenicity and reproductive/developmental toxicity databases to allow rapid access to summary toxicology information on pharmaceuticals in CDER files, with links to associated references and reviews. These databases will facilitate and improve the review process by functioning as a source of institutional memory for regulatory decision support and a resource for regulatory guidance development and scientific research.

CDER has been building a database to facilitate the review process, and in FY 1997 the Office of Pharmaceutical Science introduced the Entry Validation Application (EVA) program for electronic submissions of bioequivalence data that accompany generic drug applications. This program is now being evaluated for use with NDAs, specifically Chemistry, Manufacturing and Control (CMC) data and biopharmaceutics data. The CMC database approach should provide a mechanism for tracking information throughout the lifetime of the application. The potential outcomes of these databases include, but are not limited to, data integration, data standards, better information sharing and exchange, and better tools to facilitate the review. CDER is at the very early stages of developing this capability and is defining an approach for electronic submission of data that will provide a mechanism for tracking information throughout the lifetime of the application.

Another CDER activity involving scientific databases is the assembly of drug-drug interaction data in a unified database. This activity will make it possible to rapidly identify known and potential drug-drug interactions based on either drug substance or chemical structure.

Targeted activities for CDER's Scientific Databases are:

4 th quarter FY 2000	CDER expects to complete the assembly of the drug-drug interaction data in a unified database to facilitate retrieval and analysis by September 2000.
---------------------------------	---

4th quarter FY 2002 | CDER anticipates completing databases for all major toxicology studies submitted for drug approval, carcinogenicity, reproductive and developmental toxicity, genotoxicity, and acute/chronic toxicity studies by September 2002. Additionally, CDER expects to have defined an approach for electronic submission of data that will provide a mechanism for tracking information throughout the lifetime of the application by September 2002.

CDER Division Files System (DFS)

DFS is CDER's Electronic Document Management System (EDMS). The goal of this system is to provide an easy-to-use, automated means for creating, managing, electronic signature, and archiving of internally generated documents pertaining to the IND/NDA review process. DFS makes it possible for CDER reviewers to file reviews electronically and access historical data and consult reviewers on-line from their desktops rather than relying on paper copies. DFS Phase I was developed under PDUFA I.

Targeted activities for CDER's DFS are:

4th quarter FY 1998 | Implement Phase I of DFS. This phase provides an electronic repository for final form documents. Phase I will be deployed throughout the IND/NDA review divisions including the Office of Review Management, Office of New Drug Chemistry, and Office of Clinical Pharmacology and Biopharmaceutics.

4th quarter FY 1999 | CDER plans to complete Phase II of DFS and field version 2.0 to 1000 CDER users. DFS v2.0 is driven by the Center Director's mandate to cut document room costs by eliminating the document room's acceptance of paper review materials generated in the process of an IND or NDA review and data entry pertaining to those materials. DFS will also reduce costs by eliminating the need for document room personnel to reproduce and distribute final form copies. The scope of DFS v2.0 has been defined as providing the capability to 1) update assignment information when reviewers check in their reviews, 2) update the corporate database when an approval, not approvable, or withdrawal letter is checked into DFS for a major amendment on an NDA, 3) appending electronic signatures to documents, and 4) distributing copies of final form documents.

4th quarter FY 2000 | Concurrent to fielding DFS, CDER is working on an electronic document query project. CDER currently employs three document management solutions. Several CDER components have been using Excalibur's Electronic Filing System (EFS) to search and display documents that have been scanned and stored electronically. DFS uses Documentum's tools to track and store internally generated review documents. The EDR employs a web interface to locate documents submitted electronically. The objectives of the electronic document query project are to replace the EFS and to pilot an electronic document query and retrieval system that encompasses CDER's electronic documents and data.

CDER Corporate MIS

The Centerwide ORACLE Management Information System (COMIS) is CDER's legacy enterprise-wide MIS supporting both the pre-market and post-market regulatory activities. Information is stored in a single ORACLE database and is accessible from any personal computer or terminal in the Center. The Corporate MIS is an umbrella name for multiple applications that store and retrieve data in a single integrated database. The Corporate Database is used to track the status and progress of each submission (NDAs, INDs)

submitted to the Agency for action. It is also used to generate mandatory user fee reports and to enable tracking and milestones and workload statistics for improved management accountability. The Corporate Database is used by DFS and the EDR to prevent data redundancies and ensure data integrity.

The foundation for application development in CDER is the database. The integrity and quality of the corporate database directly impacts the usefulness of data entry and query screens and reports used by CDER personnel. To provide high quality applications and maintain and enhance them in an effective and timely manner, CDER is developing a modern, flexible, and comprehensive database structure on which to base future applications development.

CDER has formed a Corporate Database Redesign team, chaired by the Center Director, which has been conducting workshops to develop a set of functional requirements from which a data model for the redesigned database will be produced.

During this requirements development, CDER is considering the feasibility of the MIS interfacing with other systems such as ORA's Field Accomplishments and Compliance Tracking System (FACTS) to provide and track status of assignments to ORA field staff.

Targeted activities for CDER's Corporate MIS are:

4 th quarter FY 1999	CDER expects to complete the database design effort by September 1999. Schedules for subsequent phases including scheduling of interfaces with DFS and EDR will be developed immediately following completion of the design effort.
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The chart on the following page shows the schedule of CDER's system development activities.

PDUFA II Information Management Five-Year Plan (FY 1999 Revision)
July 1999

Task Name	Finish	1999				2000				2001				2002								
		Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4				
CDER EDR	Sat 9/1/01					▶																
Provide capability and capacity to accommodate full electronic NDAs	Wed 9/1/99					◆ 9/1																
Expand capability and capacity to accommodate INDs, DMFs, and Annual Reports	Sat 9/1/01													◆ 9/1								
CDER Scientific Databases	Sun 9/1/02									▶												
Complete assembly of drug-drug interaction database	Fri 9/1/00									◆ 9/1												
Complete databases for all major toxicology studies	Sun 9/1/02																	◆ 9/1				
Define approach for electronic submission of data for NDAs	Sun 9/1/02																	◆ 9/1				
CDER DFS	Fri 9/1/00	▶																				
Implement Phase I	Tue 9/1/98	◆ 9/1																				
Complete Phase II of DFS	Wed 9/1/99					◆ 9/1																
Pilot electronic document query and retrieval system	Fri 9/1/00									◆ 9/1												
CDER Corporate MIS	Wed 9/1/99					◆ 9/1																
Complete database design effort	Wed 9/1/99					◆ 9/1																

CBER Electronic Document Room (EDR)

CBER must provide a capability and the capacity to accommodate receipt and archive of electronic biologics submissions. The purpose of the EDR is to provide a facility to house the hardware and software that will store, track, and retrieve electronic documents such as the Investigational New Drug (IND) applications, Biologics Licensing Applications (BLAs), New Drug Applications (NDAs), lot release protocols, and other types of submissions. Submissions to the EDR will come in on one of several physical media types as defined in the industry guidance posted in the public docket.

Targeted activities for CBER's EDR are:

1 st Quarter FY 1999	Conduct a requirements analysis to build the foundation for beginning the design, development, and implementation activities necessary to create an EDR. Publish a Requirements Analysis and Phase I High-Level Design Analysis document for the EDR effort.
2 nd quarter FY 2000	By April 2000, CBER expects to have implemented Phase I of the EDR. In this Phase, CBER will have established the basic infrastructure for the EDR to include hardware and software architecture and security controls and some functionality such as backup, archive, and retrieval capability.
1 st quarter FY 2001	By October 2000, CBER anticipates completion of Phase II of their EDR. At completion of Phase II, CBER will have provided capability to receive and archive electronic INDs (e-INDs), integrated the EDR with RMS, and provided remote access
4 th quarter FY 2001	By September 2001, CBER plans to have completed Phase III of the EDR. With completion of Phase III, CBER will have incorporated electronic signature and secure e-mail and will have provided capability to receive and archive electronic BLAs (e-BLAs).
4 th quarter FY 2002	By September 2002, CBER plans to have completed Phase IV of the EDR. This final phase will provide enhancements and capacity upgrades and will provide the capability to receive and archive all paperless applications.

CBER Regulatory Management System (RMS)

In CBER, RMS will perform the activities of an electronic document management system as well as a management information system. RMS will be an integrated system for creating, managing and archiving internal review documents concerning a submission, as well as tracking the status of the submission. There are two primary modules of RMS. The first, RMS-IND, supports the IND process including applications and correspondence tracking. The RMS-IND module will replace CBER's legacy Biologics IND Management System (BIMS) system. The other module, RMS-BLA, incorporates the new business rules that CBER is applying to track and review BLA submissions. This module will replace the legacy Biologics Regulatory Management System (BRMS).

Targeted activities for CBER's RMS are:

4 th quarter FY 1998	By September 1998, CBER will have completed the development of the clinical trials communications in the RMS-IND module. Completing this development provided CBER with the capability to track and display clinical trial communications using Documentum.
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3 rd quarter FY 2000	By April 2000, CBER expects to have Phase I of the RMS-BLA module completed. This phase will provide CBER the functionality to process therapeutics, vaccine, and blood product submissions. Also in this phase, CBER will have completed data migration from the BRMS system.
4 th quarter FY 2001	By September 2001, CBER will have completed the enhancement of the RMS-BLA module.
1 st quarter FY 2002	In October 2001, CBER expects to have integrated the BIMS system and completed the RMS-IND module.
4 th quarter FY 2002	By September 2002, CBER will have completed Phase II of the RMS-BLA module. With completion of this phase, CBER will be able to track all applications.

CBER Document Accountability and Tracking System (DATS)

CBER is developing DATS to consolidate administrative document logging and circulation control activities by replacing two legacy systems. While DATS will be available for use by most Center employees, the primary user will be Document Control Center (DCC) personnel who will use DATS to capture receipt and document data, enter and update routing and circulation data, and maintain location and inventory information for physical files. DATS will also provide the capability to enter key information from FDA Form 1571 that is submitted by sponsors to FDA as part of an IND Original Submission or as part of an Amendment to an existing IND.

4 th quarter FY 1999	CBER is targeting implementation and fielding of DATS with the Phase I functionality by September 1999. This phase will provide the capability to capture receipt and document data and maintain location and inventory information for physical files.
3 rd quarter FY 2001	CBER will complete Phase II of DATS. Phase II will provide the capability to track routing and circulation information.

The chart on the following page shows the schedule of CBER's system development activities.

4.4 Update Technical/Non-Technical Infrastructure

ERSR Subgoal: Update the technical and non-technical infrastructure to support an electronic review environment.

Activities supporting this subgoal are associated with the technical infrastructure of the ERSR Program (e.g., acquiring, configuring, and implementing hardware and software). These often underlying activities support multiple projects and are coordinated with projects' functionality needs as appropriate. These items include standard hardware/software (e.g., desktops, network, office automation tools, servers, Internet/Intranet) needed to support system development. Activities also include additional capabilities as needed, such as a secure e-mail package for communicating with regulated industry and analytical tools needed by reviewers for use with structured databases. Other tools include library references such as the scientific Library Electronic Reference Network (LERN). Another significant activity toward meeting this subgoal involves addressing the needs for Center communication with ORA Field Offices. ORA's requirements will be integrated as appropriate with the ERSR-related functional capabilities developed in CBER and CDER.

Infrastructure also includes the foundational support aspects of the ERSR Program common to CBER, CDER, and ORA's PDUFA II IT solution:

Technical Support – Provides support to end users for hardware/software installation, software development, maintenance, and trouble shooting.

Training – Covers provision of training for development staffs and end users sufficient to ensure qualified technical support to the ERSR Program and to allow reviewers to function in an electronic review environment.

The following paragraphs provide, by PDUFA organization, planned activities for updating the technical and non-technical infrastructure to support an electronic review environment.

Center for Biologics Evaluation and Research (CBER)

Enhancing and upgrading CBER's network architecture is key to achieving the PDUFA II ERSR performance goals. CBER's current capabilities must be improved to support the proposed processes and architecture. CBER plans to upgrade network communications between all CBER locations, the network systems hardware, and desktop workstations.

The targeted activities for updating CBER's technical infrastructure are:

3 rd quarter FY 1999	Upgrade approximately 80% of the desktops within the Center to the ISA-standard desktop configuration.
	Migrate approximately 95% of its network infrastructure to ISA standards.

FY 1999	Conduct Year 2000 testing and Independent Verification and Validation (IV&V) effort to ensure that mission critical systems ³ will process dates appropriately in the year 2000.
3 rd quarter FY 1999	Certify all mission critical systems are Y2K compliant.
4 th quarter FY 1999	Upgrade networking capability by completing the installation of dark fiber between the Center's component offices. Complete the network systems hardware upgrades by September 1999, including replacing its alpha servers with NT compatible platforms.
3 rd quarter FY 2000	CBER, working with CDER, will identify and implement a secure communications solution for establishing a secure messaging capability between Agency Centers/Offices, other regulatory authorities, and the regulated industry by June 2000.

Center for Drug Evaluation and Research (CDER)

CDER is conducting several activities related to updating its technical infrastructure. A significant effort involves CDER's Enterprise Computing Architecture (ECA) which is a model that describes the relationships between the various functions within CDER. The ECA provides CDER with an enterprise-wide conceptual framework for planning information systems development.

The targeted activities for updating CDER's technical infrastructure are:

4 th quarter FY 1998	CDER defines and documents the requirements for secure electronic mail between CDER, regulated industry, and other regulatory authorities.
3 rd quarter FY 1999	Conduct a secure e-mail pilot
1 st quarter FY 1999	Publish draft Enterprise Computing Architecture Description document. This will serve as a baseline framework for planning and implementing the technical infrastructure needed to support the electronic review environment. CDER estimates that this document will represent approximately 50 percent of the ultimate scope of CDER's computing architecture.
FY 1999	Conduct an aggressive Y2K testing and IV&V effort to ensure that its mission critical systems will process dates appropriately in the year 2000.
2 nd quarter FY 1999	Certify all CDER mission critical systems are Y2K compliant.
1 st quarter FY 2000	Procure and configure the hardware and software for secure e-mail for the initial production environment.
On-going activities	Continue developing the ECA Description document, incorporating all aspects of the computing architecture. Additionally, CDER will be developing, documenting, and maintaining policies and procedures for use when developing and modifying

³ The mission critical systems associated with the ERSR development activities within CBER are Biologics IND Management System (BIMS) and the Biologics Regulatory Management System (BRMS) that are being replaced by RMS and the Document Login System (DLS) and Circulation Control System (CCS) that are being replaced by DATS.

systems within the Center's architecture.

In addition to providing the necessary resources for the operations and maintenance of the hardware and software that support the systems within the ERSR program, CDER continues to upgrade the desktops and network operations to ISA-standard configurations.

Continue providing operations and maintenance support for the technical infrastructure.

Office of Regulatory Affairs (ORA)

To fully achieve the goals of the ERSR program, ORA investigators and compliant officers in the field offices will need to access documents electronically and reduce the time to accomplish the assignments by eliminating the transit time of paper documents and task assignments. ORA envisions that they will need the capability to 1) provide each district office, each laboratory, some large resident posts on the network, and each regional office direct electronic access to the electronic documents maintained by CDER and 2) provide the ability to browse and search for the documents pre-authorized by CDER and download what they need when they need it. ORA does not require detailed access to CBER's BLA applications in the same context as in audits of CDER NDAs in accordance with CDER guidelines. One solution being considered is to provide a seamless dial-up capability to access the information needed by ORA and to have added electronic storage capability.

The targeted activities for updating ORA's technical infrastructure are:

2 nd quarter FY 1999	Complete an analysis of ORA's functional requirements for the ERSR program. This document defines the requirements of the ORA field users and provides a detailed design of an infrastructure to support the electronic receipt and retrieval of documents pertinent to investigation and compliance determination activities in the field offices.
4 th quarter FY 2002	ORA expects to design, procure, and install the necessary infrastructure to enable ORA field users to access the requisite material for conducting field inspections.

Office of Information Resources Management (OIRM)

To ensure FDA is meeting the IT requirements of FDAMA/PDUFA, OIRM is reviewing the activities within the ERSR program on a semi-annual basis. Additionally, on an as-needed basis, OIRM enlists the support of an independent reviewer to assess programmatic planning documents and other related material (from CBER, CDER, ORA, and OIRM) to identify any inconsistencies, synergies and make efficiency recommendations to senior management. In addition to planned reviews, oversight may include coordination and support of data management. This data management can include consultant support for Agency-level data modeling and data dictionary development.

The targeted activities for OIRM's oversight function are:

4 th quarter FY 1998	OIRM published the 1998 PDUFA II Information Management Five-Year Plan.
FY 1998, 1999	Oversee the Agency's Year 2000 application conversion effort. By the end of the 2 nd quarter of 1999, FDA is expected to be completed with renovation, testing, and independent verification and validation of its mission critical systems and technical infrastructure.
Semi-Annually	Request performance information from the PDUFA organizations to assess the progress of the organizations toward meeting the overall PDUFA IT goal.
Annually	Publish a yearly plan documenting the progress made to date and updating the five-year plans for future activities with the ERSR Program.

The chart on the following page shows the targeted activities for all PDUFA organizations in updating the technical/non-technical infrastructure within the ERSR program.

PDUFA II Information Management Five-Year Plan (FY 1999 Revision)
 July 1999

Task Name	Finish	1999				2000				2001				2002			
		Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	
CBER	Thu 6/1/00	[Timeline bar from Q3 1999 to Q4 2000]															
Upgrade 80% of desktops to ISA-standard desktop configuration	Tue 6/1/99				◆ 6/1												
Migrate approximately 95% of network infrastructure to ISA standards	Tue 6/1/99				◆ 6/1												
Conduct Y2K testing and IV&V of mission critical systems	Sat 5/15/99	[Shaded bar from Q3 1999 to Q2 2000]															
Certify mission critical systems are Y2K compliant	Sat 5/15/99				◆ 5/15												
Complete installation of dark fiber between CBER and component offices	Wed 9/1/99					◆ 9/1											
Define and implement a secure e-mail solution	Thu 6/1/00									◆ 6/1							
CDER	Sun 9/1/02	[Timeline bar from Q3 1999 to Q4 2002]															
Define and document requirements for secure electronic mail	Tue 9/1/98	◆ 9/1															
Conduct a secure e-mail pilot	Tue 6/1/99				◆ 6/1												
Publish draft Enterprise Computing Architecture Description document	Tue 9/1/99	◆ 9/1															
Conduct Y2K testing and IV&V of mission critical systems	Wed 3/31/99	[Shaded bar from Q3 1999 to Q2 2000]															
Certify mission critical systems are Y2K compliant	Wed 3/31/99				◆ 3/31												
Continue developing ECA description document	Sun 9/1/02	[Shaded bar from Q3 1999 to Q4 2002]															
Continue upgrading desktops and network operations to ISA standard configurations	Thu 9/30/99	[Shaded bar from Q3 1999 to Q2 2000]															
Replace obsolete disk drives, upgrade network, upgrade desktop SW, HW, replace LAN printers	Thu 12/10/98	[Shaded bar from Q3 1999 to Q2 2000]															
ORA	Sun 9/1/02	[Timeline bar from Q3 1999 to Q4 2002]															
Complete ORA's functional requirements analysis	Fri 1/1/99			◆ 1/1													
Complete design, procurement, and installation of necessary infrastructure	Sun 9/1/02															◆ 9/1	
OIRM	Mon 7/1/02	[Timeline bar from Q3 1999 to Q4 2002]															
Complete oversight of renovation, testing, and IV&V of mission critical systems	Sat 5/15/99				◆ 5/15												
Publish Annual Plan	Mon 6/3/02																
Collect Performance Information	Mon 7/1/02																
Conduct annual independent review of ERSR Program	Mon 6/3/02																

5.0 OVERALL PROGRAM OVERSIGHT

The CIO is responsible for ensuring that all PDUFA II IT investments support the Agency's common IT goals, fit into a common computing environment, and follow good IT management practices. Oversight of the ERSR Program involves integrated processes. ERSR projects are reviewed for business and technical soundness through the IT Business Planning process established by the Agency in accordance with the Clinger-Cohen Act of 1996. The ERSR Program is assessed annually by independent consultants who work with the Centers/Offices to review and assess the economic soundness of PDUFA IT investments and monitor performance in meeting established milestones.

Consistent with Department of Health and Human Services (DHHS) policies and recent legislation, including the Clinger-Cohen Act, the Agency has developed a process to become more accountable for the economic and efficient management of IT and to implement a sound and integrated IT architecture.

An integral part of the FDA business planning process is the review of the major IT investments to ensure that they are achieving defined performance goals which support the Agency mission, in terms of the project plan (i.e., milestones and resources) and expected outcomes (e.g., programmatic improvements), and are compliant with standards defined by the Agency's information systems architecture (ISA).

The IT Business Planning (ITBP) process has been utilized to review existing ERSR IT projects. The ITBP process requires the sponsoring PDUFA II Centers/Offices to prepare business cases for their IT investments. A business case is a narrative document that provides a consistent format to capture information such as business need, IT solution, costs, schedule (milestones), and performance measures.

All PDUFA II information technology investments will continue to be reviewed through this ITBP process. One major component of the ITBP process is a review of investments by a Technical Review Board (TRB) composed of Information Resource Management (IRM) Directors from each of the Centers/Offices. The goal of the TRB is to assess Agency IT investments with regard to the technical soundness of the investment, the consistency of the IT solution with the Agency's ISA, and the potential redundancy of the investment with other Agency efforts. Once the TRB has completed its assessment and determined that there are no significant technical risks that could prevent successful implementation of the IT solution, the members "credential" the investment. Though projects may be "credentialed" by the TRB, members may raise technical issues that must be addressed by project managers but do not preclude a project from proceeding.

Some PDUFA II ERSR projects are currently being defined and scoped and will be incorporated into this plan and reviewed by the TRB. Other PDUFA II items not associated with a specific project or which support multiple projects may be reviewed independently by the OCIO to ensure compliance with Agency best practices and architecture standards.

On a semi-annual basis, PDUFA organizations are asked to submit performance information. Organizations are asked to update project cost and schedule information and describe planned versus implemented functionality for each project. This information is used to develop a performance report showing progress on ERSR activities. It is also used to monitor the progress organizations are making on each of the projects and to ensure that organizations are on target to meet the overall PDUFA II IT goal.

Annually, the PDUFA II Information Management Five-Year Plan is revised to update the plans, budgets, and milestone schedules for each of the ERSR projects. This plan and the information compiled through conducting ERSR project technical reviews and developing performance reports are a means of communicating to overall Agency senior management the progress and status of the ERSR Program and

help to enable management to make informed decisions regarding funding ERSR activities. Additionally, Agency management is apprised of overall ERSR issues and activities through the Information Management Advisory Board. Through this Board, comprising both Agency management and industry representatives, collaborate on the Agency's investment of PDUFA funds toward the goal of an electronic regulatory submissions and review capability by the year 2002. The Board functions as a steering committee which ensures the PDUFA II Information Management Plan reflects the interest of all stakeholders, utilizes information management/technology best practices, and that the PDUFA II information management program implementation is consistent with that plan.

6.0 SUMMARY

The overall PDUFA goal of developing and updating information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of submissions is composed of four subgoals: developing standards; issuing guidance for regulated industry for electronic submissions; designing and implementing systems for receiving, reviewing, and tracking electronic submissions, and providing the technical and non-technical infrastructure to support an electronic review environment.

FDA organizations have planned the requisite projects and activities to meet the overall PDUFA IT goal. The organizations are participating in a variety of standards development activities and are ensuring that industry guidance for submitting applications electronically is clear, consistent, and standards-based. Efforts toward implementing systems are progressing steadily and are being supported continuously by upgrades to desktop and network infrastructure.

Throughout the life-cycle of the ERSR Program, FDA organizations will collaborate on system development activities where appropriate. Existing systems and those being developed or re-engineered within the ERSR program are Center-specific due to differing business needs created by statutes and mandates. For example, firms are required to submit a separate application for each therapeutic biological and human drug product. But each application for a blood product, vaccine, or allergenic may contain multiple products; and one product may receive approval while another does not. This situation necessitates unique counting and tracking mechanisms that are not applicable to all applications. Each Center has developed internal business processes designed to meet their unique regulatory review requirements, and these processes dictate their applications development. However, their corporate database structures are very similar and allow for the data to be shared. Therefore, the technical architecture for both is largely the same and consistent with the Agency's Information Systems Architecture (ISA) program. If submissions enter the Agency based on the published electronic submission guidance, differences in the systems between Centers will not affect regulated industry.

A significant portion of the efforts expended in FY 1999 across the Agency are toward ensuring that systems and infrastructure (both PDUFA and non-PDUFA related) are not vulnerable to the Year 2000 (Y2K) date change. Over the past two years, the FDA has been engaged in an intensive effort that has required a significant expenditure of resources aggressively addressing Y2K issues on multiple fronts: systems, telecommunications, desktop, biomedical and facilities. Of chief importance to the Agency has been the impact of the Y2K issue on its mission-critical functions. Consequently, all efforts were prioritized to ensure neither the Agency nor the public is at risk as a result of the date change. During the latter part of FY 1998 and throughout FY 1999, FDA worked diligently to renovate, validate, and implement Y2K compliant systems and successfully met deadlines established by OMB for completing these activities.

As a result of the pressure imposed by the Y2K focus, several of the systems development projects were put on hold or delayed during FY 1999. Additionally, a few of the ERSR projects are still in a very early development stage and schedules for the life-cycle phases and integration with other projects have not been completed. The largest of the systems development projects are very extensive in scope and cover both PDUFA and non-PDUFA related regulatory activities. PDUFA-related (i.e., pre-market) components within these systems are being given the highest priority to meet the overall PDUFA IT goal of having an ability to receive and process submissions electronically by FY 2002.

APPENDIX A
ERSR PROGRAM BUDGET

PDUFA II Information Management Progress Report
July 1999

CBER	FY1998 PLANNED	FY1999 PLANNED	FY2000 PLANNED	FY2001 PLANNED	FY2002 PLANNED	TOTAL PLANNED
EDR						
	\$ 1,338	\$ 1,235	\$ 543	\$ 474	\$ 474	\$ 4,064
Industry Guidance						
	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Other Information Document Management Systems						
	\$ 757	\$ 1,054	\$ 850	\$ 605	\$ 551	\$ 3,817
Other Initiatives (Technical Infrastructure)						
	\$ 2,230	\$ 1,928	\$ 1,495	\$ 1,132	\$ 966	\$ 7,751
RMS						
	\$ 3,575	\$ 3,683	\$ 2,040	\$ 2,200	\$ 2,200	\$ 13,698
Standards						
	\$ 50	\$ 125	\$ 125	\$ 125	\$ 125	\$ 550
CBER SubTotal						
	\$ 7,950	\$ 8,025	\$ 5,053	\$ 4,536	\$ 4,316	\$ 29,880

CDER	FY1998 PLANNED	FY1999 PLANNED	FY2000 PLANNED	FY2001 PLANNED	FY2002 PLANNED	TOTAL PLANNED
Corporate MIS						
	\$ 1,982	\$ 3,297	\$ 2,303	\$ 1,384	\$ 1,385	\$ 10,351
EDMS/DFS						
	\$ 2,407	\$ 1,804	\$ 1,904	\$ 1,254	\$ 1,254	\$ 8,623
EDR						
	\$ 613	\$ 707	\$ 490	\$ 490	\$ 490	\$ 2,790
Industry Guidance						
	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Other Initiatives (Technical Infrastructure)						
	\$ 7,116	\$ 5,176	\$ 4,876	\$ 3,266	\$ 3,321	\$ 23,755
Scientific Databases						
	\$ 420	\$ 730	\$ 785	\$ 510	\$ 380	\$ 2,825
Standards						
	\$ 150	\$ 285	\$ 160	\$ 160	\$ 160	\$ 915
Reserve						
			\$ 2,050	\$ 1,150	\$ 1,150	\$ 4,350
CDER SubTotal						
	\$ 12,688	\$ 11,999	\$ 12,568	\$ 8,214	\$ 8,140	\$ 53,609

ORA	FY1998 PLANNED	FY1999 PLANNED	FY2000 PLANNED	FY2001 PLANNED	FY2002 PLANNED	TOTAL PLANNED
Requirements Analysis						
	\$ 165	\$ -	\$ -	\$ -	\$ -	\$ 450
Design and Implementation						
	\$ 360	\$ 80	\$ 986	\$ 773	\$ 971	\$ 3,045
ORA SubTotal						
	\$ 525	\$ 80	\$ 986	\$ 773	\$ 971	\$ 3,335

PDUFA II Information Management Progress Report
 July 1999

	FY1998 PLANNED	FY1999 PLANNED	FY2000 PLANNED	FY2001 PLANNED	FY2002 PLANNED	TOTAL PLANNED
CBER						
	\$ 7,950	\$ 8,025	\$ 5,053	\$ 4,536	\$ 4,316	\$ 29,880
CDER						
	\$ 12,688	\$ 11,999	\$ 12,568	\$ 8,214	\$ 8,140	\$ 53,609
ORA						
	\$ 525	\$ 80	\$ 986	\$ 773	\$ 971	\$ 3,335
Center Total						
	\$ 21,163	\$ 20,104	\$ 18,607	\$ 13,523	\$ 13,427	\$ 86,824

OIRM	FY1998 PLANNED	FY1999 PLANNED	FY2000 PLANNED	FY2001 PLANNED	FY2002 PLANNED	TOTAL PLANNED
Oversight and Coordination						
	\$ 438	\$ 547	\$ 1,954	\$ 1,092	\$ 750	\$ 4,781
Grand Total						
	\$ 438	\$ 547	\$ 1,954	\$ 1,092	\$ 750	\$ 4,781

Note: OIRM oversight and coordination activities are funded from overhead funds.

APPENDIX B

ACRONYMS

Acronyms

AERS	Adverse Event Reporting System
AMF	Administrative Management of Files
ANDA	Abbreviated New Drug Applications
BA/BE	Bioavailability/Bioequivalency
BER	Blood Establishment Registration System
BIMO	Biomedical Research Monitoring
BLA	Biologic License Applications
BRMS	Biologics Regulatory Management System
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDR	Central Document Room
CIO	Chief Information Officer
CMC	Chemistry, Manufacturing and Controls
COMIS	Corporate Oracle Management Information System
COTS	Commercial Off-the-Shelf
CRF	Case Report Form
CRT	Case Report Tabulations
CTD	Common Technical Documents
CVM	Center for Veterinary Medicine
DATS	Document Accountability and Tracking System
DCC	Document Control Center
DFS	Division File System
DIA	Drug Information Association
DMF	Drug Master File
DSS	Decision Support System
EDI	Electronic Data Interchange
EDMS	Electronic Document Management System
EDR	Electronic Document Room
EES	Establishment Evaluation System
EFOIA	Electronic Freedom of Information Act
ERS	Electronic Regulatory Submission
ERSR	Electronic Regulatory Submission and Review
EVA	Entry Validation Application
EWG	Expert Working Group
FACTS	Field Accomplishments and Compliance Tracking System
FDA	Food and Drug Administration
FDAMA	FDA Modernization Act
FOI	Freedom of Information
FTE	Full-time Equivalent
GPRA	Government Performance and Results Act

ICH	International Conference on Harmonization
IIS	Internet Information Server
IM	Information Management
IMAB	Information Management Advisory Board
IND	Investigational New Drug
IRM	Information Resources Management
ISA	Information Systems Architecture
IT	Information Technology
ITBP	Information Technology Business Planning
ITCC	IT Coordinating Committee
IV&V	Independent Verification and Validation
LERN	Library Electronic Reference Network
LRS	Lot Release System
M2	ICH M2 Expert Working Group (EWG) focusing on Electronic Standards for Transmission of Regulatory Information
M4	ICH M4 EWG focuses on Common Technical Documents (CTD) for the technical content of sections of the NDA
MIS	Management Information System
NDA	New Drug Application
NOS	Network Operating System
NPR	National Performance Review
OC	Office of the Commissioner
OHRMS	Office of Human Resources and Management Services
OIRM	Office of Information Resources Management
OMS	Office of Management and Systems
ORA	Office of Regulatory Affairs
PDF	Portable Data Format
PDUFA	Prescription Drug User Fee Act
PhRMA	Pharmaceutical Research and Manufacturers of America
PLA	Product License Applications
RAC	Regulatory Affairs Committee
RMS	Regulatory Management System
TBD	To Be Determined
TCP/IP	Transmission Control Protocol/Internet Protocol
TRB	Technical Review Board
Y2K	Year 2000

