



# PDUFA II Five-Year Plan

*FY 2001 Update*

1998 - 1999 - 2000 - **2001** - 2002

**Department of Health and Human Services**  
**FOOD AND DRUG ADMINISTRATION**  
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## **Executive Summary**

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The Prescription Drug User Fee Act of 1992 (PDUFA I) provided additional resources 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 and extended it through September 30, 2002 (PDUFA II). PDUFA II commits FDA to even faster review goals for some applications, new goals for meetings and dispute resolution, and the electronic receipt and review of applications by the end of FY 2002.

In July 1998, FDA completed the original PDUFA II Five-Year Plan. It 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 third annual update.

The Secretary's transmittal letter for our FY 2000 financial report recently stated that one of the biggest concerns FDA faces is the erosion of core resources. This has been caused by both (1) PDUFA requirements to increase spending on drug review from appropriations each year and (2) the fact that the agency has repeatedly not been given increased appropriations to cover the cost of pay and other cost increases. This is being addressed with the submission of President Bush's FY 2002 budget. This plan assumes future funding to cover pay increases.

The changes to this update are minor compared with last year's revisions. Total staffing will increase by 365 FTE's for the centers and ORA by FY 2002. These are increases over FY 1997 staffing levels at the end of PDUFA I. Increases from 1997 staffing levels by component follow:

- CDER—an increase of 280 FTE's by the end of 5 years (compared with an increase of 240 FTE's in the original plan and an increase of 234 in last year's update);
- CBER—a net increase of 85 FTE's by the end of 5 years (compared with an increase of 57 FTE's in the original plan and an increase of 79 in last year's update); and
- ORA—level staffing by the end of 5 years (compared with an increase of 28 FTE's in the original plan, and level staffing in last year's update).

Revenues are re-estimated at about \$5 million less than in last year's update. Staffing increases are possible, even though revenues are reduced, because FDA will spend all of the money it collects each year, plus about \$36 million of carry-over balances, in the final two years of PDUFA II. Increased spending is essential to meet the PDUFA II goals that become increasingly difficult in the final 2 years of PDUFA II. However, carryover balances by the end of FY 2002 are now estimated at less than \$22 million. This low level of carryover funds at the end of FY 2002 make it imperative that PDUFA be reauthorized before September 30, 2002, to avoid a funding hiatus if PDUFA II expires before reauthorization is enacted.

Of the total planned spending, 59 percent will be allocated for employee salary and benefit costs. Center and ORA operating funds and IT investments will each use 12%. Of the total, CDER will spend 58%, CBER will spend 21%, and ORA will spend 6%. Overhead will use 8% of the funds, centrally funded items will use 5%, and rent payments to GSA will use 3%.

Operating at these levels should enable the agency to meet PDUFA goals through FY 2002.

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## Purpose

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In 1998 FDA developed the *PDUFA II Five-Year Plan* as a blueprint for investing the substantial resources the agency expected to collect under the recently reauthorized Prescription Drug User Fee Act (PDUFA II). FDA's purpose in developing the plan was to ensure that fee revenues would be effectively used to meet the challenging new goals associated with PDUFA II. The plan allocated the resources expected each year among the FDA components responsible for achieving PDUFA goals. FDA committed to update the plan annually as changes in workload and revenues replace original estimates, unanticipated contingencies occur, and technology evolves. FDA also made the plan, and subsequent updates, publicly available for anyone to review and comment on.

The most recent plan Update is always the basis for the initial allocation of fee resources among FDA components each fiscal year. Thus the plan enables prompt allocation of funds at the beginning of each new fiscal year. Adjustments may still be made later in the fiscal year when the plan is updated again.

This FY 2001 Update is the third annual revision since the original plan was published in 1998, and reflects actual resource use through FY 2000, adjustments in assumptions, and updated projections for revenue and spending through the end of PDUFA II—September 30, 2002.

## **Background**

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### **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 from 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 goals for the program. By 1997, fees provided FDA with an additional \$87.5 million a year for the drug evaluation process.

FDA primarily spent these new resources to hire additional 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. Since 1994, FDA has submitted annual PDUFA Performance and Financial Reports to Congress on progress in meeting performance goals and the use of fees. (See <http://www.fda.gov/oc/pdufa/reports.html>)

FDA's success in ensuring that these resources were well used was recognized in late 1997 when FDA received the prestigious Innovations in American Government Award, jointly sponsored by the Ford Foundation and the Harvard University's John F. Kennedy School of 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 review process improvements.

### **PDUFA II**

As a result of this success PDUFA was reauthorized and extended through September 30, 2002. This extension authorizes FDA to collect and spend fee revenue 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, amended and extended 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 increasingly stringent goals.

## PDUFA II Goals

The goals for PDUFA II are challenging, diverse, and resource intensive. Major components of the review process must be even faster. Many of the goals required the development of guidance documents and databases to track performance. Goals were 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 is also required. The following table provides an overview and comparison of the major goals by the end of PDUFA I and at the end of PDUFA II. For more detail on the actual goals and FDA's performance, see FDA's latest Performance Report on the Internet at <http://www.fda.gov/oc/pdufa/reports.html>.

**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 the end of FY 2002

## FY 2001 Update

When the *PDUFA II Five-Year Plan* was originally published in July 1998, FDA committed to annual reviews and adjustments as actual spending and revenue amounts replace earlier estimates, unanticipated contingencies occur, and technology evolves. This FY 2001 Update is the third update since the original plan was developed and published. Some of the assumptions in the next section have changed as a result of our experience through the end of FY 2000.

Since 1998, FDA has used linear regression analysis to estimate the number of fee-paying applications and application fee revenues. Under PDUFA formulas, the estimate of revenue for fee-paying applications is used to set product and establishment fees—each of them is set to generate the same amount of revenue as application fees. In this Update annual revenue forecasts are down slightly, and planned expenditures are up slightly.

FDA's application workload forecasts and fee levels for FY 2001 were published in a *Federal Register* notice on December 18, 2000 (Attachment 1). Extending the same linear regression line depicted in that Federal Register notice, the forecast of fee-paying applications and revenues through FY 2002 is updated in this plan revision. Due to a slight decrease in workload estimates, the revenues forecast for FY 2001 and 2002 have decreased slightly from last year's projections. Workload and inflation estimates are discussed (Assumption 2, page 6), and their cumulative impact is summarized in the PDUFA II Fee and Revenue Estimation Worksheet (Attachment 2).

Expenditure forecasts have increased modestly in this FY 2001 Update. These increases are essential so that FDA may hire sufficient staff to cope with the increasingly challenging PDUFA II goals. Increasing spending while revenue decreases is possible because carryover balances—funds collected in previous years but not spent—are available; these carryover balances are being utilized during the final three years of PDUFA II.

This FY 2001 Update retains the same basic format that was used last year.

## Assumptions

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This plan is based on ten major assumptions. Each was reassessed for FY 2001. Most are unchanged or have minor adjustments since year's Update. However, assumptions 3 and 8 have been significantly revised since last year. A discussion of all ten assumptions follows.

**1. The increased staffing and support 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, and are referred to as the **PDUFA I Additive Base**. In 1997, two-thirds of these funds were spent on pay and benefits for an additional 659 Full Time Equivalents (FTE's) in CDER, CBER and ORA. These were above the staffing level FDA had been devoting to the review of human drug and biologic applications in FY 1992, the year before PDUFA was enacted. 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 each year was crucial to FDA's ability to review drug and biologic applications rapidly. These resources are the foundation upon which the improvements mandated by PDUFA II are built.

In FY 2000 three additional FTE's were transferred to CDER from the Ombudsman's Office as part of the reorganization of the Office of the Commissioner. These were formerly paid from PDUFA overhead funds from the PDUFA I Additive Base, but are now considered as a center component of the PDUFA I Additive Base, bringing the total to 662. PDUFA II ensures that these 662 FTE's (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 (although further adjustments allocations may be made if warranted by workload or other changes):

**PDUFA I Additive Base FTE's by Component**

Year	CDER	CBER	ORA	Total
1998	398	187	74	659
1999	418	167	74	659
2000 and Beyond	421	167	74	662

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

- Future annual pay and benefit cost increases of 5.88 percent (based on past experience)
- Center support costs of \$9,000 per FTE annually
- ORA's support costs of \$16,000 annually per FTE (largely due to travel costs for pre-approval inspections)
- Center support costs included research support funds for CBER of \$590,000 in 1998 and \$295,000 in 1999. Research funding from fees was discontinued after 1999.
- Overhead is calculated as a percent of center/ORAs pay and benefits. (Overhead calculations are discussed beginning on page 23.)
- Central account and rent estimates are based on previous actual costs and future estimates are inflated at 5 percent annually, based on past experience.

Actual costs for maintaining the PDUFA I Additive Base are provided through FY 2000 and estimates are made for FY 2001 and 2002. This year's updated projections, below, are very close to last year's estimates.

**PDUFA I Additive Base Fund Estimates (\$000)**

<b>Item</b>	<b>1998 Actual</b>	<b>1999 Actual</b>	<b>2000 Actual</b>	<b>2001 Plan</b>	<b>2002 Plan</b>	<b>Total <sup>1</sup></b>
<b>Pay and Benefits for 662 Center/ORAs FTE's</b>	\$56,993	\$60,280	\$63,945	\$67,705	\$71,686	\$320,608
<b>Center/ORAs Support</b>	\$7,246	\$6,749	\$6,476	\$6,476	\$6,476	\$33,423
<b>Overhead</b>	\$10,753	\$9,869	\$8,614	\$9,121	\$9,657	\$48,014
<b>Central Accounts</b>	\$5,521	\$4,687	\$6,469	\$6,792	\$7,132	\$30,600
<b>Rent</b>		\$1,140	\$1,197	\$1,256	\$1,319	\$4,912
<b>Total <sup>1</sup></b>	<b>\$80,513</b>	<b>\$82,725</b>	<b>\$86,700</b>	<b>\$91,350</b>	<b>\$96,270</b>	<b>\$437,557</b>

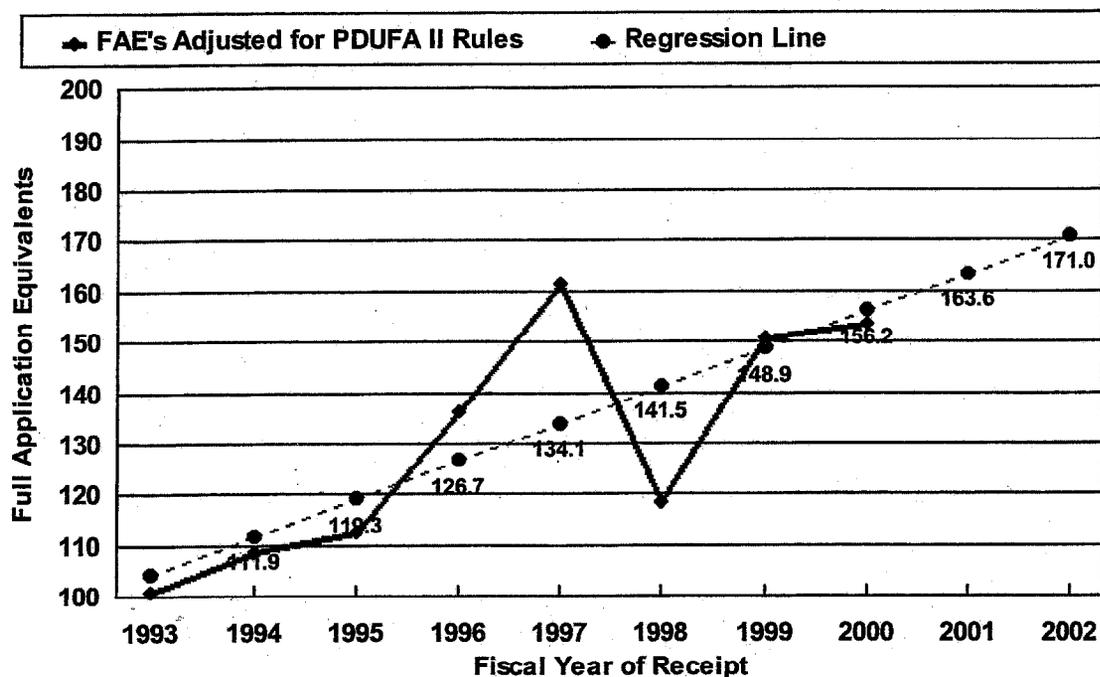
<sup>1</sup> Numbers may not add due to rounding.

2. **Fee revenue estimates are based on annual increases of about 5 percent in fee-paying applications and a 3.7 percent in inflation.**

Since 1998 FDA has used linear regression analysis to estimate the number of fee-paying applications and application fee revenues for the next year, and to set product and establishment fees for the next year. That linear regression analysis is updated and published annually in the *Federal Register*—most recently on December 18, 2000 (Attachment 1). Using that same data and method to estimate fee-paying applications and revenues through FY 2002 projects an increase of about 5 percent, as depicted in the graph that follows.

## Fee-Paying Full Application Equivalents

Using 1993-2000 Data, Adjusted for PDUFA II Rules



Based on the regression line shown above, and estimating the inflation adjustment for next year at 3.7 percent (the current estimate for the FY 2002 federal pay increase, which is the driver for fee adjustments), FDA updated its projection of fee revenues. The more detailed projection from which the table below is summarized is included in Attachment 2.

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

Numbers May Not Add Due to Rounding

Item	1998	1999	2000	2001	2002	Total
<b>Fees—Original 1998 Plan</b>	\$117,122	\$132,273	\$145,435	\$167,168	\$177,915	\$739,913
<b>Fees—Current FY 2001 Update</b>	\$117,122	\$122,012	\$137,699	\$149,273	\$159,097	\$685,202
<b>Difference</b>		(\$10,261)	(\$7,736)	(\$17,895)	(\$18,818)	(\$54,711)

As a result of this reassessment of potential revenues through FY 2002, this revised five-year plan assumes that revenue collections will be \$55 million less than originally planned—rather than \$50 million less as envisioned in last year's plan update.

**3. In each of the next 2 years FDA will spend substantially more than it collects in fees, utilizing carryover balances available from previous years.**

Any PDUFA fees FDA collects but does not obligate by the end of the fiscal year are "carried over" for use in a future fiscal year. FDA has spent less than it collected in several previous years, but began spending these carry-over balances in FY 2000. FDA began FY 2001 with a carryover balance of over \$57.4 million. This will permit FDA to spend more than it collects in each of the next two years.

In both FY 2001 and 2002, FDA plans to spend about \$18 million more than it collects, in order to assure that the agency has the staffing levels and support it needs to meet the PDUFA goals.

Operating this way will result in substantially lower carryover balances when PDUFA II expires on September 30, 2002. The agency has decided it is more prudent to utilize these carryover balances during the final two years of PUDFA II, to assure goals are met, than it would be to conserve the resources and risk failing to meet the goals. A further discussion of carryover balances is contained on pages 26.

**4. About \$247 million in new fee revenue will be available over 5 years.**

Subtracting the amount needed to sustain the PDUFA I Additive Base (Assumption 1) from the total revenues FDA expects to have available each year (Assumption 2) results in the net new revenue available for allocation to meet the PDUFA II goals. This is the amount available from PDUFA II fees for additional investments over 5 years to meet the PDUFA II goals.

**Revenues Anticipated and Net New Resources Available for PDUFA II (\$000)**

Item	1998	1999	2000	2001	2002	Total
Fees Anticipated	\$117,122	\$122,012	\$137,699	\$149,273	\$159,097	\$685,202
PDUFA I Additive Base	\$80,513	\$82,725	\$86,700	\$91,350	\$96,270	\$437,557
Net New Resources	\$36,609	\$39,287	\$50,999	\$57,923	\$62,827	\$247,645

Over five years, this is a little less (\$5.7 million) than estimated in last year's plan Update. It represents about a 13 percent reduction from the \$284 million originally planned in 1998. However, spending from the carryover balances (Assumption 3) will still permit five-year spending at close to the levels originally envisioned in the original 1998 plan.

**5. As in the original plan, it is assumed that all statutory conditions or "triggers" necessary for PDUFA to operate will be met each year.**

The law allows FDA to collect and spend PDUFA II revenues each year only if three specific conditions are met. This plan assumes that each of the three statutory conditions will be met each year:

- Total FDA appropriations (exclusive of user fees and rent) each year must total at least as much as FDA received in 1997, with some adjustments. Those amounts are:

<b>Fiscal Year</b>	<b>1997 Amount (\$ Millions) Less Rent and User Fees</b>	<b>Adjustment Factor</b> (Actual factors through FY 2001, estimated for FY 2002)	<b>Minimum Appropriation (\$ Millions)</b>	<b>Actual Appropriation (\$Millions) Less Rent and Fees</b>
1998	\$820	1.0000	\$820	\$858
1999	\$820	1.0144	\$832	\$888
2000	\$820	1.0375	\$851	\$940
2001	\$820	1.0687	\$876	\$964
2002	\$820	1.0932	\$896	

This trigger is easily met, even though FDA has not received increases to cover the cost of pay increases and inflation for its core programs for eight years—which was the original intent of this trigger—because FDA has received appropriation increases earmarked for specific initiatives since 1997 (e.g., food safety, tobacco, etc.).

- Each year FDA must actually spend at least as much from appropriations on the human drug review process as it spent from appropriations on this process in 1997, with some adjustments.

<b>Fiscal Year</b>	<b>1997 Amount Spent on Drug Review from Appropriations (\$ Millions)</b>	<b>Adjustment Factor</b> (Actual factors through FY 2001, and estimated for FY 2002)	<b>Minimum Drug Review Spending from Appropriations (\$ Millions)</b>	<b>Actual Drug Review Spending from Appropriations (\$Millions)</b>
1998	\$148	1.0000	\$148	\$152
1999	\$148	1.0144	\$150	\$160
2000	\$148	1.0375	\$154	\$168
2001	\$148	1.0687	\$158	
2002	\$148	1.0932	\$162	

If this trigger is not met, even by one dollar, no fees may legally be collected or spent for the year. This is the most difficult of the triggers for FDA to meet. FDA will not know exactly how much it has spent from appropriations until after the end of the year when final accounting reports are prepared. FDA plans to spend this minimum from appropriations each year. Because of the unforgiving nature of this trigger, FDA must spend more than the minimum, just to be sure that the trigger is met when the final accounting is done. The result is troublesome. Even when most FDA programs do not receive appropriations to cover costs of inflation and mandatory pay increases, core FDA programs other than drug review have to be cut even more to assure that appropriated

spending for drug approval meets the statutory minimum (including an inflation increase) required by this trigger.

- PDUFA fee revenues may be collected and spent only to the extent provided each year in FDA's appropriation. If collections exceed appropriations, the surplus can be kept by FDA and used to reduce anticipated collections in a future year.

<b>Fiscal Year</b>	<b>PDUFA Fees Provided in Appropriations (\$Millions)</b>	<b>PDUFA Fees Actually Collected (\$Millions) as of 9/30/2000</b>	<b>Overage, if Any (\$Millions)</b>
1998	\$117	\$117	
1999	\$132	\$122	
2000	\$145	\$138	
2001	\$149 <sup>1</sup>		
2002	\$162		

<sup>1</sup> FDA's FY 2001 appropriation specifies \$149 million, but data available after that budget request was submitted indicate that up to \$154 million may be collected in FY 2001. Collecting and keeping this larger amount for FY 2001 use would require a supplemental appropriation.

**6. 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 are not 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. The amount FDA pays for rent for PDUFA is no longer capped and increases must be paid from fees.**

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.

Beginning in FY 1999, the Appropriation Act for FDA no longer contained that cap. Instead FDA's Appropriation Act 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 paid to GSA doubled in FY 1999—increasing from \$46.3 million in FY 1998 to \$88.3 million. This impacted all programs, including the human drug review process. The share of rent payable for the human drug review process from PDUFA revenue increased by \$5.4

million in FY 1999, and increases each year with inflation and space increases necessary to accommodate the growing drug review staff.

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

<b>Rent Paid to GSA</b>	<b>1998 Actual</b>	<b>1999 Actual</b>	<b>2000 Actual</b>	<b>2001 Plan</b>	<b>2002 Plan</b>
<b>Rent From Appropriation</b>	\$6,245	\$7,817	\$8,772	\$8,640	\$8,750
<b>From PDUFA Fees</b>	\$0	\$5,428	\$5,643	\$5,860	\$6,240
<b>Total Rent Paid to GSA</b>	\$6,245	\$13,245	\$14,415	\$14,500	\$14,990

**8. No amount will be held in a contingency reserve for FY 2002.**

The likelihood of unanticipated events increases the further the plan tries to project into the future. In the early years of the plan, substantial contingency reserves were included for out-years. Now that we are in the final two years of the plan, no contingency reserve is set aside. Carry-over balances should cover any contingencies that arise.

**9. By the end of PDUFA II, total spending from all sources for the human drug application review process will have increased by about 46 percent.**

This FY 2001 update is based on the total revenues shown in the table below.

**Projection of Total Funds Spent for the Human Drug Application Review Process (\$000)**

<b>Source of Funds</b>	<b>1997 Actual</b>	<b>1998 Actual</b>	<b>1999 Actual</b>	<b>2000 Actual</b>	<b>2001 Estimate</b>	<b>2002 Estimate</b>
<b>S&amp;E Appropriations<sup>1</sup></b>	\$147,959	\$151,836	\$159,670	\$167,646	\$158,119	\$161,756
<b>Fees from Industry</b>	\$84,289	\$101,615	\$122,515	\$147,276	\$167,544	\$176,896
<b>Total Funds<sup>2</sup></b>	\$232,249	\$253,452	\$282,185	\$314,922	\$325,663	\$338,652

<sup>1</sup>Total includes Rent Appropriation in 1997 and 1998. Beginning in 1999 the Rent Appropriation was consolidated into the Salaries and Expenses Appropriation. Amounts for FY 2001 and 2002 are current estimates 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.

<sup>2</sup>Numbers may not add due to rounding.

PDUFA revenues will increase by about 46 percent over the 5 years of this program—from \$232 million in 1997 to about \$339 million in 2002. This increase by itself may seem quite large. However, the combined impact of increased workload and pay increases over the five years is actually a little less than the compounded increase in workload and inflation that

FDA has experienced. Workload and inflation increases alone, when compounded, exceed 47 percent over 5 years. This means that the total resources available for drug review have almost, but not quite, kept pace with the combined growth in workload and inflationary cost increases.

**10. The plan will be reassessed and updated 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 29.

## **Planning Process**

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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 adjusters to achieve those goals that were enacted in the statute.

The initial PDUFA II Five-Year Plan, completed in July 1998, reflected the resources initially anticipated and FDA plans for investing those resources. The plan has been a living and dynamic document, and has been updated annually. Responding to changes in revenue forecasts, subsequent plans have first reduced, and then expanded, expenditure projections, based on latest submission and workload trends. At this time, spending levels projected over the five years of PDUFA II are close to the five-year level initially planned.

For this FY 2001 plan update, the Office of Management and Systems (OMS) again 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. CDER, CBER and ORA were each asked to reassess essential needs in order to ensure that they meet the PDUFA II goals, which become increasingly challenging in the final years. Some increases in staffing were deemed essential for CDER and CBER, and are reflected in this revised plan. Higher levels of spending have been planned for the final two years of PDUFA II to enable the centers and ORA to meet these goals. These higher levels of spending are possible because: (1) some funds originally planned for earlier years were not used, and remain available; (2) costs of maintaining the PDUFA I additive base are less than originally forecast; and (3) overhead costs have substantially decreased.

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 also identifies Electronic Regulatory Submission and Review (ERSR) accomplishments to date.

The overall PDUFA II Five-Year Plan update 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 this year and next year and provide an Overhead Summary 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**

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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 \$180 million—an increase of \$16 million above the original plan and \$13 million above last year's update. A year-by-year resource summary of CDER's plan is on page 16. 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 plan is for funds to retain current staff and to hire and support additional staff for the drug evaluation process. This represents \$95 million (53 percent) of CDER's total plan and will enable CDER to add 280 more FTE's to the drug review process since the beginning of PDUFA II in FY 1998. Much of the FY 2001 increase will be used to hire additional staff to manage the increased workload associated with pre-approval inspections and clinical investigator inspections.

This number is in addition to CDER's appropriated drug review base of 749 FTE's and the PDUFA I additive base of 421 FTE's paid from fees—for a total of 1,450 CDER FTE's dedicated to the drug review process by FY 2002.

The additional personnel will be used to achieve the Center's expedited new drug evaluation performance goals for NDA's, efficacy supplements, manufacturing supplements, and resubmissions of original NDA's as established under PDUFA II. Recognizing that it takes 12 to 24 months for new employees to become proficient reviewers, CDER is attempting to hire most of the new staff by the end of fiscal year 2001. This level of staffing will allow staff to be trained and to handle the increased workload associated with PDUFA II goals and increasing workload during the final year of PDUFA II.

The Personnel and Support subtotal also includes funds to acquire more space for this additional staff—about \$700,000 over the final two 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 \$33.4 million (19 percent of the total plan) for this purpose through FY 2002. These improvements span many offices that 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, enhance 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 \$51.6 million (29 percent of the total) for IT enhancements for the drug review process. This includes four parts: (1) funds to develop the capability for electronic application receipt and review by FY 2002 which account for \$20.6 million; (2) funds for replacing CDER's management information system which account for \$8.1 million; (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 \$20.4 million over 5 years; and (4) funds obligated at the agency level by the Office of the Chief Information Officer in support of CDER IT needs which account for \$2.5 million.

The table on the following page summarizes CDER's revised plans to invest the additional funds made available under PDUFA II.

**FY 2001 Five-Year Plan Update**

**CDER Plan Summary Tables--PDUFA II  
Plan for Funds from PDUFA Fee Revenues (\$000)**

Note: Numbers Are Rounded and May Not Add

Category	1998 Actual	1999 Actual	2000 Actual	2001 Plan	2002 Plan	5-Year Total
<b>PDUFA I Additive Base</b>						
PDUFA I Additive Base FTE's <sup>1</sup>	398	418	421	421	421	
Payroll for PDUFA I FTE's	\$36,847	\$40,150	\$42,721	\$45,233	\$47,893	\$212,844
Operating Support for PDUFA I Base	\$3,493	\$3,805	\$3,789	\$3,789	\$3,789	\$18,665
<b>Subtotal--To Maintain PDUFA I Levels</b>	<b>\$40,340</b>	<b>\$43,955</b>	<b>\$46,510</b>	<b>\$49,022</b>	<b>\$51,682</b>	<b>\$231,509</b>
<b>PDUFA II Enhancements Over PDUFA I</b>						
Additional FTE's Planned	49	70	183	257	280	
(Increment Each Year)	49	21	116	74	23	
Total PDUFA Additive FTE's in This Plan. <sup>2</sup>	447	488	604	678	701	
Payroll for Additional FTE's <sup>3</sup>	\$4,162	\$6,112	\$17,378	\$26,476	\$30,395	\$84,523
Operating Support for Additional FTE's <sup>4</sup>	\$0	\$1,108	\$819	\$1,638	\$2,520	\$6,085
Startup Costs for New FTE (One-time) <sup>5</sup>	\$0	\$861	\$285	\$0	\$0	\$1,146
Recruit/Relocation/Renos/Security	\$752	\$418	\$593	\$650	\$500	\$2,913
OMS Reserve for Additional Space			\$2	\$330	\$350	\$682
<b>Subtotal--Personnel and Support</b>	<b>\$4,914</b>	<b>\$8,499</b>	<b>\$19,077</b>	<b>\$29,094</b>	<b>\$33,765</b>	<b>\$95,349</b>
ICH Support <sup>6</sup>	\$174	\$96	\$274	\$420	\$420	\$1,384
Redesign of Sci. Review Process	\$1,284	\$6,658	\$6,894	\$9,002	\$8,186	\$32,024
<b>Subtotal--Process Enhancements</b>	<b>\$1,458</b>	<b>\$6,754</b>	<b>\$7,168</b>	<b>\$9,422</b>	<b>\$8,606</b>	<b>\$33,408</b>
Electronic Submissions	\$2,934	\$4,128	\$4,137	\$5,298	\$4,115	\$20,612
Document Management	\$773	\$2,660	\$2,243	\$224	\$2,175	\$8,075
Other Electronic Initiatives <sup>7</sup>	\$3,811	\$3,920	\$4,928	\$3,837	\$3,904	\$20,400
Expenditures by OCIO			\$1,861	\$338	\$344	\$2,544
<b>Subtotal--Information Technology</b>	<b>\$7,518</b>	<b>\$10,708</b>	<b>\$13,169</b>	<b>\$9,697</b>	<b>\$10,538</b>	<b>\$51,631</b>
<b>Subtotal PDUFA II Enhancements</b>	<b>\$13,890</b>	<b>\$25,961</b>	<b>\$39,414</b>	<b>\$48,213</b>	<b>\$52,909</b>	<b>\$180,388</b>
<b>Total PDUFA Additive Funds--CDER</b>	<b>\$54,230</b>	<b>\$69,916</b>	<b>\$85,924</b>	<b>\$97,236</b>	<b>\$104,591</b>	<b>\$411,897</b>

<sup>1</sup> Payroll Base is for 398 FTE's in 1998, 418 in 1999 (20 FTE's Transferred from CBER); and 421 thereafter (3 from Ombudsman).

<sup>2</sup> PDUFA Additive FTE Base (top line) plus Additional FTE Planned amount shown above.

<sup>3</sup> Salary and benefits estimates based on \$93,550 in FY 2000 and escalated at 5.88% thereafter. The FY 1998, 1999, and 2000 amounts are actual expenses.

<sup>4</sup> Operating Support per FTE is calculated at \$9,000 per year.

<sup>5</sup> \$9,500 per FTE is provided in first year only for start-up costs.

<sup>6</sup> Estimate only: Actual distribution of ICH funds will be decided each year by the Office of International and Constituent Relations.

<sup>7</sup> Includes \$150,000 for enhancing either CDER or ORA automated system for tracking bioresearch monitoring inspections

## **CBER Plan Summary**

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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 \$60.1 million—an increase of \$1.9 million above the original 1998 plan and \$5.4 million above the level planned in last year's update. A year-by-year resource summary of CBER's plan is on page 19. 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 CBER's plan is for funds to hire and support additional staff for the drug evaluation process. This represents \$22.9 million (37 percent) of CBER's total plan and will enable CBER to have a net increase of 85 more FTE's to the drug review process by FY 2002.

This number is in addition to the PDUFA I additive base of 167 FTE's and CBER's appropriated PDUFA base of 292 FTE's --for a total PDUFA effort of 544 FTE's a year by FY 2002.

In CBER's plan the additional FTE's needed each year were arrayed with the specific PDUFA II goals. The PDUFA II performance goals are much more demanding than the PDUFA I goals. Review times for standard applications are reduced gradually from 12 months to 10 months so that by FY 2002, 90% of the applications must be reviewed within 10 months after receipt. While the 6-month review performance goals for priority applications became effective in FY 1997, no additional resources were received to accomplish that commitment. Experience has shown that priority application review requires more resources than standard applications. Because of the intensity of application review effort required for priority applications, personnel are not available to perform other necessary tasks such as meeting with sponsors of pending applications, reviewing clinical hold responses, or providing special protocol assessments.

The Managed Review Process must now be expanded to incorporate the IND sub-process. The rollout of the Managed Review Process to include the IND sub-process began in January 1998. There are payroll and operating costs associated with the rollout of the Managed Review Process. The successful accomplishment of the PDUFA II commitments depends upon the expansion of this process.

Pre-IND and the first 30-days of IND review are included in the new drug review process under PDUFA II. In addition to the application review workload, there are several other PDUFA II commitments, which require resources. Continued enhancements are needed to the

CBER Regulatory Meetings Database (CRMTS) which tracks industry's requests for formal meetings with the Center, and captures information necessary to measure performance.

### **Review Process Enhancements**

The second component of CBER's plan is funding for enhancements to the application review process. CBER's plans \$5.4 million over 5 years (9 percent of the total plan) for this purpose. These improvements span several offices that contribute to attaining PDUFA II goals. Included are funds to train reviewers, increase pre-approval inspections, and cost increases for CBER's Document Control Center related to increasing application volume and the transition to electronic applications.

The Lot Release System for PDUFA products requires review and analysis to determine if the current database information can be integrated or new databases need to be developed. The ICH travel funds reflect FY 1998, 1999, and 2000 actual costs and estimates for FY 2001 and 2002. 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 remains the largest part of CBER's plan -- \$ 32.8 million (54 percent of the total plan). It has four parts: (1) funds to develop the capability for electronic application receipt and review by FY 2002 account for \$6.1 million; (2) funds for replacing CBER's document tracking system with state-of-the-art capabilities account for \$19.9 million; (3) funds for other IT enhancements that support the PDUFA II goals (such as overall maintenance and upgrading of CBER's data systems and networks that support PDUFA) account for \$6.3 million over 5 years; and (4) funds obligated at the agency level by the Office of the Chief Information Officer in support of CBER IT needs account for \$516,000.

The funding for electronic submissions will enable CBER to comply with the Agency's initiative to develop and update its information management infrastructure to allow, by FY 2002, the paperless receipt and processing of IND's and human drug (including biologics) applications, as defined in PDUFA, and related submissions.

The table on the following page summarizes CBER's revised plans to invest the additional funds made available under PDUFA II.

## **ORA Plan Summary**

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ORA has developed an amended, detailed overall plan for the 5 years of PDUFA II, reflecting the revised resource level estimates. The revised plan totals \$5.5 million--a decrease of \$7.8 million below the original 1998 plan and of \$0.4 million below the level planned in last year's update. A year-by-year resource summary of ORA's plan is on page 22. It has the same three principal components as the center plan: (1) personnel and support, (2) review process enhancements, and (3) information technology.

### **Personnel and Support**

Most of the field PDUFA costs are based on the 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 are not spread equally over the year. Both assignments and reporting ebb and flow during the year. Again in FY2000 an unusually large proportion of PDUFA reimbursable time was reported not only late in the fiscal year, some of it after the PDUFA time reporting deadline. This, in addition to the implementation of a new field information system, resulted in delayed time reports. ORA is determined to monitor and adjust PDUFA time use reports in FY2001 so that system implementation problems and delayed reporting are not reflected in PDUFA time reported.

An analysis of field PDUFA time use has led to the current estimate of resource use for the remaining portion of PDUFA II. Over the last 4 years, an increasing number of PDUFA decisions were based on paper reviews using the ORA Profiles database on inspections. CDER's Office of Compliance increasingly uses field data to conduct paper reviews 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. As field related PDUFA assignments are increasing, the trend is to use alternatives to requiring inspections, which is moderating the use of PDUFA resources. Consequently, our plan calls for a stable level of 74 fee funded FTE's for the remaining years of PDUFA II.

ORA expects to expend a total of 180 FTE's on the drug review process in each of the remaining two years of the plan (74 FTE's paid from PDUFA fees and 106 FTE's paid from appropriations).

### **Review Process Enhancements**

The second component of ORA's plan is funding for enhancements to processes that support pre-approval inspection work. This will account for \$3.9 million over 5 years. These enhancements include equipment, training, and better time reporting. Inadequate laboratory equipment to analyze samples collected during pre-approval inspections has delayed field completion of some pre-approval inspection work. Therefore, ORA plans \$203,000 to purchase

specific pieces of equipment required to analyze pre-approval inspection samples. ORA also plans \$140,000 for PDUFA related training. ORA's training needs are exacerbated because the 180 staff-years devoted to PDUFA represent time spent by about 600 different employees. Training and refresher courses for those that conduct PDUFA pre-approval inspections or analyze samples collected have to be provided to most of these 600 individuals who contribute to the 180 FTE's of PDUFA work. The amount requested for training will meet this need.

ORA plans \$1,000,000 in FY 2001 to upgrade the Field Accomplishments and Compliance Tracking System (FACTS) by developing and implementing a new time accounting reporting module comparable to the CDER and CBER systems. During FY2000, ORA contracted with SRA International, Inc. to conduct a requirements analysis and to develop summary reports of FACTS data that will permit ORA to more accurately monitor time and track accomplishments. The initial requirements analysis has been completed. The first of these summary reports is scheduled for delivery in March of FY2001. A prototype of expanded information is scheduled for delivery and preliminary implementation in the first quarter of FY2002.

### **Information Technology**

The final component of ORA's plan is funding to continue electronic document management implementation at the field office level, upgrade desktops and laptops for PDUFA staff, and to upgrade bandwidth and network services for field offices. In addition, these funds will allow ORA to develop and update its information management infrastructure to allow paperless application processing. This will entail about \$2.5 million over five years.

To fulfill ORA's PDUFA review responsibilities for performing pre-market inspections or recommending decisions on a firm's ability to adequately manufacture a product, ORA investigators and compliance officers in the field offices need to access documents electronically. Each district office, laboratory, regional office, and some resident posts must be provided access to the electronic documents maintained by CDER. It is critical that ORA field offices have the ability to browse and search for authorized documents so that work can meet PDUFA timeframes. Now that CDER's review-related data systems have reached their maturity, CDER and ORA are assessing the infrastructure necessary to permit ORA field personnel to electronically access the required documents. By the end of the second quarter FY2001, ORA and CDER will have determined the best information access methodology for use by field personnel. The infrastructure and security design and implementation plan will be complete by the third quarter; implementation will begin in the fourth quarter of FY2001. Plans are for complete access to be achieved by the fourth quarter FY2002.

The table on following page summarizes ORA's updated plans to invest the additional funds made available under PDUFA II.

FY 2001 Five-Year Plan Update

**ORA Plan Summary Tables--PDUFA II**  
**Plan for Funds from PDUFA Fee Revenues (\$000)**

Note: Numbers Are Rounded and May Not Add

Category	1998 Actual	1999 Actual	2000 Actual	2001 Plan	2002 Plan	5-Year Total
<b>PDUFA Additive FTE Base</b>	74	74	74	74	74	
Base Payroll for 74 FTE (5% Inflation)	\$5,049	\$5,296	\$5,668	\$6,001	\$6,354	\$28,367
Base Operating Funds (3% Inflation)	\$1,234	\$1,119	\$1,184	\$1,184	\$1,184	\$5,905
<b>Subtotal--To Maintain PDUFA I Levels</b>	<b>\$6,283</b>	<b>\$6,415</b>	<b>\$6,852</b>	<b>\$7,185</b>	<b>\$7,538</b>	<b>\$34,272</b>
<b>PDUFA II Enhancements over PDUFA I</b>						
Additional FTE Requested	0	-12	0	0	0	
(Increment Each Year)	0	-12	12	0	0	
Total PDUFA Additive FTE's in this Plan <sup>†</sup>	74	62	74	74	74	
Additional FTE Payroll <sup>2</sup>	\$0	(\$739)	\$0	\$0	\$0	(\$739)
Support Costs @ \$9,000/FTE	\$0	(\$108)	\$0	\$0	\$0	(\$108)
FTE Start-up Costs <sup>3</sup>	\$0	\$0	\$0	\$0	\$0	\$0
<b>Subtotal--Personnel and Support</b>	<b>\$0</b>	<b>(\$847)</b>	<b>\$0</b>	<b>\$0</b>	<b>\$0</b>	<b>(\$847)</b>
ICH Travel	\$9	\$4	\$8	\$0	\$0	\$21
Equipment	\$141	\$378	\$193	\$203	\$218	\$1,133
Training	\$21	\$248	\$564	\$140	\$184	\$1,157
FACTS Upgrade to Monitor/Track Time		\$37	\$513	\$1,000	\$0	\$1,550
<b>Subtotal--Process Enhancements</b>	<b>\$171</b>	<b>\$667</b>	<b>\$1,278</b>	<b>\$1,343</b>	<b>\$402</b>	<b>\$3,861</b>
Electronic Submissions	\$165	\$80	\$0	\$0	\$0	\$245
Document Management		\$0	\$0	\$50	\$260	\$310
Other Electronic Initiatives	\$347	\$0	\$64	\$823	\$711	\$1,945
<b>Information Technology <sup>4</sup></b>	<b>\$512</b>	<b>\$80</b>	<b>\$64</b>	<b>\$873</b>	<b>\$971</b>	<b>\$2,500</b>
<b>Total PDUFA II Enhancements</b>	<b>\$683</b>	<b>(\$100)</b>	<b>\$1,342</b>	<b>\$2,216</b>	<b>\$1,373</b>	<b>\$5,514</b>
<b>Total PDUFA Additive Funds--ORA</b>	<b>\$6,966</b>	<b>\$6,315</b>	<b>\$8,194</b>	<b>\$9,401</b>	<b>\$8,911</b>	<b>\$39,786</b>

<sup>1</sup> PDUFA Additive FTE Base (preceding line) plus additional FTE's included in this plan.

<sup>2</sup> ORA pay and benefits estimates based on FY 2000 costs of \$71,700 per FTE increasing at 5.88% thereafter.

<sup>3</sup> \$9,500 per FTE is provided only in first year an FTE is added to cover one-time start-up costs.

<sup>4</sup> This line does not include \$150,000 in CDER plan for enhancing either CDER or ORA automated tracking system for clinical trials inspections.

## Overhead Summary

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

### 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 Office of the Commissioner (OC) overhead costs. For this discussion, OC is used in its larger sense to encompass the several management and staff offices that report to the Commissioner. That formula conforms with generally accepted accounting principles and was found reasonable by Arthur Andersen consultants in subsequent annual audits. The formula is:

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

The salary costs used in this formula do not include the costs of any benefits. 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 FY 2000, FDA spent a total of \$314.9 million on the drug review process as defined in PDUFA, and the FY 2000 PDUFA overhead costs were \$25.5 million, or about 8.1 percent. This is down from 10.4 percent in 1998 and 11.1 percent in 1993, due in large part to the reorganization and reduction of the Office of the Commissioner late in FY 1999. This revised plan assumes the same low rate—8.1 percent of total PDUFA spending for FY 2001 and FY 2002. The FY 2001 overhead for the drug review process is estimated to be about \$26.5 million. Over the five year period, this plan reflects about \$15.9 million less for PDUFA overhead from fees 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 FY 2001 is \$14.3 million.

The difference between the total estimated overhead costs of \$26.5 million in FY 2001 and the \$14.3 million that must be paid from appropriated funds is \$12.2 million. This \$12.2 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 that follows.

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

<b>Source</b>	<b>1998 Actual</b>	<b>1999 Actual</b>	<b>2000 Actual</b>	<b>2001 Estimate</b>	<b>2002 Estimate</b>
<b>S&amp;E Appropriations</b>	\$15,291	\$14,683	\$14,182	\$14,332	\$14,500
<b>PDUFA Fees</b>	\$10,753	\$9,869	\$11,353	\$12,170	\$13,067
<b>Total Overhead</b>	<b>\$26,044</b>	<b>\$24,552</b>	<b>\$25,534</b>	<b>\$26,502</b>	<b>\$27,567</b>

The aggregate result of these revised estimates is a reduction in fee revenue spent on overhead. The five-year overhead total from fees in this FY 2001 plan update is \$57.2 million—compared to \$73.1 million estimated in the original plan and \$59.5 million estimated in last year's plan update. Most of this saving comes from the reorganization and streamlining of the Office of the Commissioner. The result is more of the fee revenue available for increased review and support staff in the centers and ORA.

**Use of Overhead Funds**

Beginning in FY 2000, all overhead costs paid from PDUFA fees are now treated as indirect costs. The fees allocated to PDUFA overhead are used to pay for the same percent of the costs of all components of the Office of the Commissioner. For FY 2001, approximately \$12,170,000 in fees from PDUFA will pay for about 13 percent of total OC overhead costs. Since OC will utilize about 808 FTE's in FY 2001, PDUFA fees will pay for 13 percent of these FTE, or about 105 FTE.

## FDA Plan Summary

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The Agency plan for PDUFA II is a composite of plans developed by CDER, CBER, and ORA. Tables 1-7 on pages 27 and 28 summarize the overall FDA plan. The discussion below summarizes information in each of these tables.

- Table 1 (page 27) shows the \$438 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 \$247 million over the 5 years.
- Table 2 (page 27) shows the allocation of \$278 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 total line allocates all the PDUFA funds, above the PDUFA I Additive Base, that FDA expects to spend through FY 2002.
- Table 3 (page 27) shows the allocation of this \$278 million by expense category. About \$105 million will be spent for pay and benefits for a net of 365 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, and rent. 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 Actual	1999 Actual	2000 Estimate	2001 Estimate	2002 Estimate
<b>CDER</b>	+49	+70	+183	+257	+280
<b>CBER</b>	-9	+28	+37	+85	+85
<b>ORA</b>		-12			
<b>Total</b>	+40	+86	+220	+342	+365

- Table 4 (page 28) 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 FY 2001, FDA will spend about \$18.3 million more than it expects to collect and in FY 2002 about \$17.8 million more. FDA can do this because FY 2001 began with about \$57.4 million in PDUFA carryover funds. These carryover balances will be spent down in the last two years of the program so that FDA can hire the additional personnel necessary to continue to meet PDUFA goals. The table below reflects planned carryover balances.

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

Item	2001	2002
<b>Carryover Balance—Beginning of Year</b>	\$57,368	\$39,097
<b>Amount of Carryover Used</b>	\$18,271	\$17,800
<b>Carryover Balance—End of Year</b>	\$39,097	\$21,298

Unfortunately, reducing the carryover balances is essential for the agency to have sufficient operating funds to enable the agency to accomplish PDUFA goals. However, the low level of carryover balances at the end of PDUFA II will mean that it is essential for PDUFA reauthorization to be completed before September 30, 2002, so that the agency will have adequate funding as FY 2003 begins.

- Tables 5 and 6 (page 28) summarize the allocation of the \$716 million in total fee revenue that FDA plans to spend over the 5 years of PDUFA II (PDUFA I additive base plus PDUFA II increases) by component (Table 5) and by expense category (Table 6). The last column in both tables shows the percent of total PDUFA funds planned over the next 5 years. By component, CDER will be allocated 58 percent, CBER 21 percent, ORA 6 percent, overhead 8 percent, central accounts 5 percent, and rental payments to GSA 3 percent. By other expense categories, 59 percent of the total PDUFA II revenues will be dedicated to pay and benefits for staff (same as in the original plan), 12 percent for center/ORR operating costs, 12 percent for IT.
- Table 7 (page 28) 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 2001 Five-Year Plan Update**  
**FDA Plan Summary Tables--PDUFA II (\$000)**

Note: Numbers Are Rounded and May Not Add

**Table 1: PDUFA I Additive Base, and Estimated Funds Available**

Item\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate	Five-Year Total	Five-Year Percent
Pay and Benefits for Centers/ORAs	\$56,993	\$60,280	\$63,945	\$67,705	\$71,686	\$320,608	73%
Base Operating Funds--Centers/ORAs	\$7,246	\$6,749	\$6,476	\$6,476	\$6,476	\$33,423	8%
Overhead	\$10,753	\$9,869	\$8,614	\$9,121	\$9,657	\$48,014	11%
Central Accounts	\$5,521	\$4,687	\$6,469	\$6,792	\$7,132	\$30,600	7%
Rent		\$1,140	\$1,197	\$1,256	\$1,319	\$4,912	
<b>Total--PDUFA I Additive Base</b>	<b>\$80,513</b>	<b>\$82,725</b>	<b>\$86,700</b>	<b>\$91,350</b>	<b>\$96,270</b>	<b>\$437,557</b>	<b>100%</b>
Estimated Fee Receipts	\$117,122	\$122,012	\$137,699	\$149,273	\$159,097	\$685,202	
Available for Enhancements	\$36,609	\$39,287	\$50,999	\$57,923	\$62,827	\$247,645	

**Table 2: Funds Planned for Enhancements--by Component**

Component\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate	Five-Year Total	Five-Year Percent
CDER	\$13,890	\$25,961	\$39,414	\$48,213	\$52,909	\$180,388	65%
CBER	\$6,529	\$9,641	\$12,546	\$16,297	\$16,134	\$61,147	22%
ORA	\$683	(\$100)	\$1,342	\$2,216	\$1,373	\$5,514	2%
Overhead	\$0	\$0	\$2,739	\$3,049	\$3,410	\$9,198	3%
Central Accounts	\$0	\$0	\$88	\$1,814	\$1,880	\$3,782	1%
Rental Payments to GSA	\$0	\$4,288	\$4,446	\$4,604	\$4,921	\$18,259	7%
Contingency Reserve	\$0	\$0	\$0	\$0	\$0	\$0	0%
<b>Total</b>	<b>\$21,102</b>	<b>\$39,790</b>	<b>\$60,575</b>	<b>\$76,194</b>	<b>\$80,627</b>	<b>\$278,289</b>	<b>100%</b>

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

Expense Category\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate	Five-Year Total	Five-Year Percent
Pay and Benefits for Centers/ORAs	\$4,162	\$6,508	\$20,843	\$34,306	\$38,685	\$104,504	38%
Support Costs for Personnel	\$455	\$2,279	\$2,191	\$3,839	\$4,135	\$12,899	5%
Process Enhancements	\$2,397	\$8,424	\$10,652	\$11,505	\$9,701	\$42,679	15%
IT	\$14,088	\$18,291	\$19,616	\$17,077	\$17,895	\$86,967	31%
<b>Subtotal to Centers</b>	<b>\$21,102</b>	<b>\$35,502</b>	<b>\$53,302</b>	<b>\$66,727</b>	<b>\$70,416</b>	<b>\$247,049</b>	<b>89%</b>
Overhead	\$0	\$0	\$2,739	\$3,049	\$3,410	\$9,198	3%
Central Accounts	\$0	\$0	\$88	\$1,814	\$1,880	\$3,782	1%
Rental Payments to GSA	\$0	\$4,288	\$4,446	\$4,604	\$4,921	\$18,259	7%
Contingency Reserve	\$0	\$0	\$0	\$0	\$0	\$0	0%
<b>Total</b>	<b>\$21,102</b>	<b>\$39,790</b>	<b>\$60,575</b>	<b>\$76,194</b>	<b>\$80,627</b>	<b>\$278,289</b>	<b>100%</b>

**FY 2001 Five-Year Plan Update**  
**FDA Plan Summary Tables--PDUFA II (\$000)**

Note: Numbers Are Rounded and May Not Add

**Table 4: Difference Between Plans & Available Funds, with Year-end Carry-Over Balances**

Category\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate
Difference Between Plan & Available				(\$18,271)	(\$17,800)
Est. Carry-Over Balance-Year Beginning				\$57,368	\$39,097
Est. Carry-Over Balance-Year End	\$67,518	\$71,584	\$57,368	\$39,097	\$21,298

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

Component\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate	Five-Year Total	Five-Year Percent
CDER	\$54,230	\$69,916	\$85,924	\$97,236	\$104,591	\$411,897	58%
CBER	\$24,145	\$26,300	\$29,605	\$34,271	\$35,076	\$149,397	21%
ORA	\$6,966	\$6,315	\$8,194	\$9,401	\$8,911	\$39,786	6%
Overhead	\$10,753	\$9,869	\$11,353	\$12,170	\$13,067	\$57,212	8%
Central Accounts	\$5,521	\$4,687	\$6,557	\$8,606	\$9,011	\$34,383	5%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,240	\$23,171	3%
Contingency Reserve	\$0	\$0	\$0	\$0	\$0	\$0	0%
<b>Total</b>	<b>\$101,615</b>	<b>\$122,515</b>	<b>\$147,276</b>	<b>\$167,544</b>	<b>\$176,896</b>	<b>\$715,846</b>	<b>100%</b>

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

Expense Category\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate	Five-Year Total	Five-Year Percent
Pay and Benefits for Centers/ORA	\$61,153	\$66,788	\$84,788	\$102,011	\$110,371	\$425,111	59%
Operating Funds--Excluding IT	\$10,100	\$17,452	\$19,319	\$21,820	\$20,312	\$89,003	12%
Information Technology	\$14,088	\$18,291	\$19,616	\$17,077	\$17,895	\$86,967	12%
Overhead	\$10,753	\$9,869	\$11,353	\$12,170	\$13,067	\$57,212	8%
Central Accounts	\$5,521	\$4,687	\$6,557	\$8,606	\$9,011	\$34,383	5%
Rental Payments to GSA	\$0	\$5,428	\$5,643	\$5,860	\$6,240	\$23,171	3%
Contingency Reserve	\$0	\$0	\$0	\$0	\$0	\$0	0%
<b>Total</b>	<b>\$101,615</b>	<b>\$122,515</b>	<b>\$147,276</b>	<b>\$167,544</b>	<b>\$176,896</b>	<b>\$715,846</b>	<b>100%</b>

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

FTE Category\Year	1998 Actual	1999 Actual	2000 Actual	2001 Estimate	2002 Estimate
Base FTE's Paid from Appropriations	1,147	1,147	1,147	1,147	1,147
PDUFA I Additive Base FTE's	659	659	662	662	662
FTE's Added for PDUFA II	40	86	220	342	365
<b>Total</b>	<b>1,846</b>	<b>1,892</b>	<b>2,029</b>	<b>2,151</b>	<b>2,174</b>

## **Annual Reassessments**

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As originally envisioned, this plan will continue to be revised each year based on the latest information available. This third annual plan update is intended to let the centers and ORA know the amounts to expect in FY 2001 and 2002. This information facilitates the resource acquisition and planning for center work required to meet the PDUFA II goals. Actual workload and revenues will continue to be monitored closely.

The plan is a dynamic framework for the investments FDA must make. It will be updated again in the second quarter of FY 2002. Like previous updates, that final update will take into account the actual accomplishments, workload, revenues, and expenses of the previous fiscal years and the planned accomplishments, workload, revenues and fees to be charged in the final year. Workload and revenue estimates are always based on the information set forth in the latest *Federal Register* notice setting fees.

If revenues are expected to be at levels lower than the assumptions of this plan then cutbacks in hiring and other expenses will be required, as was the case in the 1999 revision. On the other hand, if available PDUFA revenues exceed planned amounts because of carry-over balances available, increased workload estimates, and/or higher inflation adjustments, the additional revenues will be allocated, as was the case in the FY 2000 update. Also, if reassessments of center/ORAs PDUFA workload indicate that PDUFA workload is out of kilter with the distribution of resources in this plan, then adjustments may be made.

Because FDA plans to spend all funds it expects to collect, adjustments needed by the centers and ORA each year will generally be within the total amounts already planned for the 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.

authorities. The guidance on the overall strategy for the evaluation of veterinary drug residues in human food (VICH Guidance on General Testing Approach) will be made available at a later time. This guidance was developed after consideration of the existing ICH guidances for pharmaceuticals for human use: "Genotoxicity: A Standard Battery of Genotoxicity Testing of Pharmaceuticals" and "Guidance on Specific Aspects of Regulatory Genotoxicity Tests for Pharmaceuticals." Account was also taken of the Organisation for Economic Cooperation and Development methodological guidances and of the current practices for evaluating the safety of veterinary drug residues in human food in the European Union, Japan, the U.S.A., Australia, and New Zealand.

Comments about the draft guidance documents will be considered by the FDA and the VICH Safety Working Group. Ultimately, FDA intends to adopt the VICH Steering Committee's final guidances and publish them as future guidance. (Information collection is covered under OMB No. 0910-0117. Information collection also could be covered by OMB No. 0910-0032.)

### III. Significance of Guidance

This draft guidance document, developed under the VICH process, has been revised to conform to FDA's good guidance practices regulation (65 FR 56468, September 19, 2000). For example, the documents have been designated "guidance" rather than "guideline." Because guidance documents are not binding, unless specifically supported by statute or regulation, mandatory words such as "must," "shall," and "will" in the original VICH documents have been substituted with "should." Similarly, words such as "require" or "requirement" have been replaced by "recommendation" or "recommended" as appropriate to the context.

The draft guidance document represents the agency's current thinking on genotoxicity safety studies for veterinary drug residues in human food. This guidance document does not create or confer any rights for or on any person and will not operate to bind FDA or the public. An alternative method may be used as long as it satisfies the requirements of applicable statutes and regulations.

### IV. Comments

This draft guidance document is being distributed for comment purposes only and is not intended for implementation at this time. Interested persons may

submit to the Dockets Management Branch (address above) written comments regarding this draft guidance document. Submit written comments by January 17, 2001, to ensure adequate consideration in preparation of the final guidance. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. A copy of the draft guidance document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: December 8, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00-32113 Filed 12-15-00; 8:45 am]

BILLING CODE: 4160-01-S

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### Establishment of Prescription Drug User Fee Rates for Fiscal Year 2001

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) 2001. 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 2001 were set by the PDUFA, as amended, 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:** Frank P. Claunts, Office of Management and Systems (HF-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4427.

#### SUPPLEMENTARY INFORMATION:

##### I. Background

The PDUFA (Public Law 102-571), as amended by the FDAMA (Public Law

105-115), referred to as the PDUFA II in this document, 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 FY 1998 through 2002, under the PDUFA II, the application fee rates are set in the statute, but are to be adjusted annually for cumulative inflation since FY 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.

Each year from FY 1998 through 2002, FDA is required to set establishment fees and product fees so that the estimated total fee revenue from each of these two categories will equal 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 2001 for application, establishment, and product fees. These fees are retroactive to October 1, 2000, and will remain in effect through September 30, 2001. For fees already paid on applications and supplements submitted on or after October 1, 2000, 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, 2000, the new fee schedule must be used. Invoices for establishment and product fees for FY 2001 will be issued in December 2000, using the new fee schedule.

##### II. Inflation and Workload Adjustment Process

The PDUFA II 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) (all items; U.S. city average), or (2) the total percentage pay change for that FY for Federal employees stationed in the Washington, DC, metropolitan area. The PDUFA II provides for this annual adjustment to be cumulative and compounded annually after 1997 (see 21 U.S.C. 379h(c)(1)).

The PDUFA II 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 II 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 PDUFA II 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 PDUFA II 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 for safety or effectiveness (other than bioavailability or bioequivalence studies) (21 U.S.C. 379h(a)(1)(A) and 379h(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 above are set out in the PDUFA II for FY 2001 (\$267,606 for applications requiring clinical data, and \$133,803 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, or (2) the total percentage pay change for that FY for Federal employees stationed in DC, as adjusted for any locality-based payment. The PDUFA II 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) or the increase in applicable Federal salaries (2.45 percent).

The adjustment for FY 1999 was 3.68 percent (63 FR 70777 at 70778, December 22, 1998). This was the greater of the CPI increase for FY 1998 (1.49 percent) or the increase in applicable Federal salaries (3.68 percent).

The adjustment for FY 2000 was 4.94 percent (64 FR 72669 at 72670, December 28, 1999). This was the greater of the CPI increase for FY 1999 (2.62 percent) or the increase in applicable Federal salaries (4.94 percent).

The adjustment for FY 2001 is 3.81 percent. This is the greater of the CPI increase for FY 2000 (3.45 percent) or the increase in applicable Federal salaries (3.81 percent).

Compounding these amounts (1.0245 times 1.0368 times 1.0494 times 1.0381) yields a total compounded inflation increase of 15.71 percent for FY 2001. The adjusted application fee rates are computed by adding one to the decimal equivalent of this percent (0.1571) and multiplying this amount (1.1571) by the FY 2001 statutory application fee rates stated above (\$267,606 for applications requiring clinical data, and \$133,803 for applications not requiring clinical data or supplements requiring clinical data). For FY 2001 the adjusted application fee rates are \$309,647 for applications requiring clinical data, and \$154,823 for applications not requiring clinical data or supplements requiring clinical data. These amounts must be submitted with all applications during FY 2001.

#### B. Estimate of Total Application Fee Revenue

Total application fee revenues for FY 2001 will be estimated by multiplying the number of fee-paying applications FDA receives in FY 2001 (from October 1, 2000, through September 30, 2001) 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 FY 2001

application fee revenues. To do this FDA first determines its FY 2000 fee-paying full application equivalents, and uses that number in a linear regression analysis to predict the number of fee-paying full application equivalents expected in FY 2001. This is the same technique applied in each of the previous 2 fiscal years.

In FY 2000, FDA received and filed 117 human drug applications that require clinical data for approval, 21 that did not require clinical data for approval, and 131 supplements to human drug applications that required 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, 2000, FDA refused to file, or firms withdrew before filing, 11 applications that required clinical data, and 5 applications that either did not require clinical data or that were supplements requiring clinical data. The full applications refused for filing or withdrawn before filing pay one-fourth the full application fee and are counted as one-fourth of an application; the applications that do not require clinical data and the supplements refused for filing or withdrawn before filing pay one-eighth of the full application fee and are each counted as one-eighth of an application.

Using this methodology, the number of full application equivalents that were submitted for review in FY 2000 was 196.4, before any exemptions, waivers or reductions. Under the PDUFA II, FDA waives application fees for certain small businesses submitting their first application and for certain orphan products. Certain application supplements for pediatric indications are also exempt from fees. In addition, the PDUFA II provides a number of other grounds for waivers (public health necessity, preventing significant barriers to innovation, and fees exceed the cost). In FY 2000 waivers or exemptions were applied to 42.9 full application equivalents (14 for orphan products, 8 for small businesses, 12.5 for pediatric supplements, and 8.4 miscellaneous exemptions/waivers). Therefore, for FY 2000, FDA estimates that it received the equivalent of 153.5 (196.4 minus 42.9) full application equivalents that will

pay fees, after allowing for exemptions, waivers and reductions.

A linear regression line based on the adjusted number of fee-paying full

application equivalent submissions since 1993, and including our FY 2000 total of 153.5 fee-paying full application equivalents, projects the receipt of 163.6

fee-paying full application equivalent (FAE) submissions in FY 2001, as reflected in table 1 of this document and graph below.

TABLE 1.

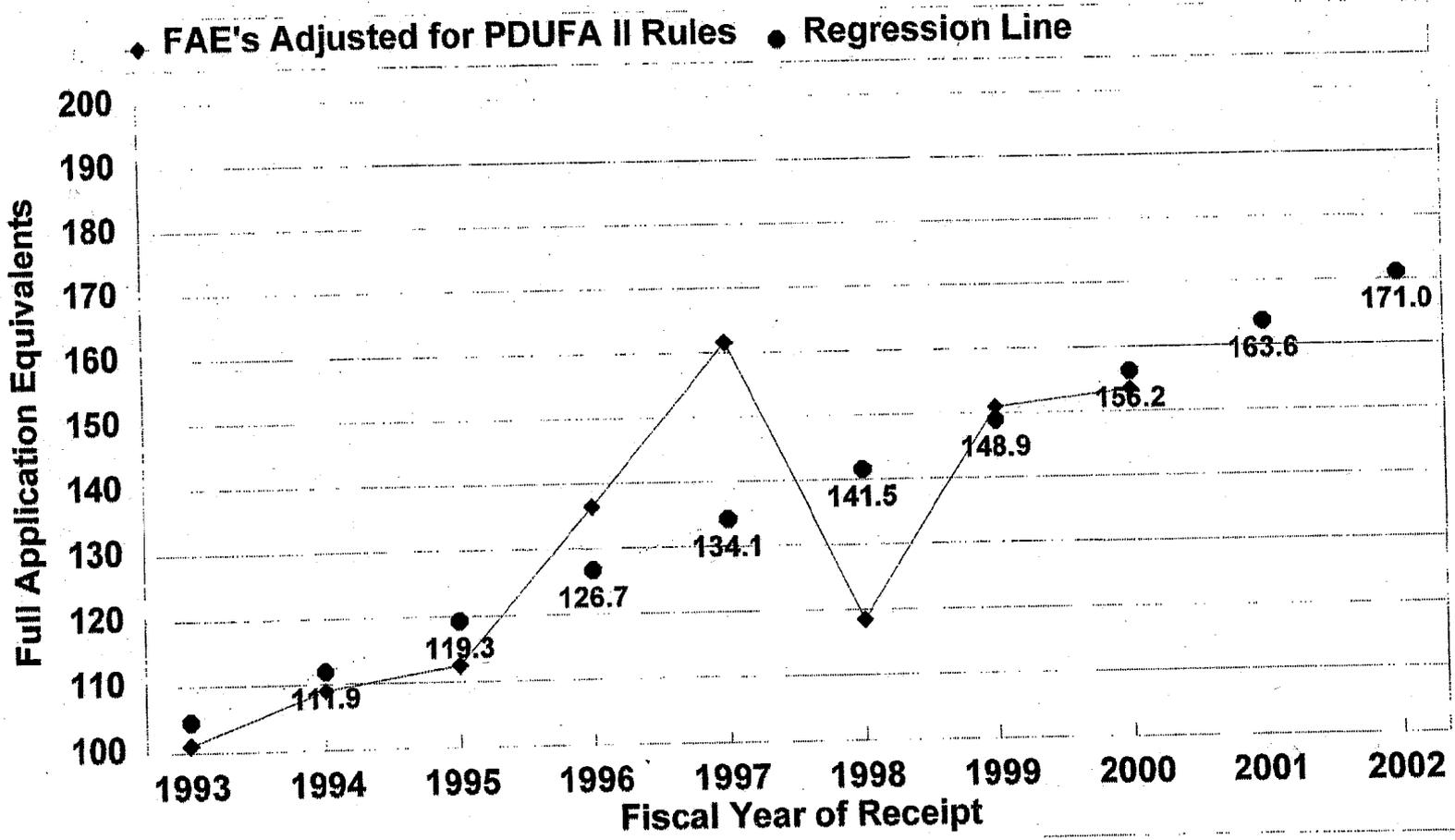
Fiscal Year	1993	1994	1995	1996	1997	1998	1999	2000	2001
Adjusted fee-paying FAE's	101.0	108.9	112.5	136.3	161.5	118.5	150.9	153.5	
Regression line	104.5	111.9	119.3	126.7	134.1	141.5	148.9	156.2	163.6

BILLING CODE 4160-01-F

Regression Analysis/Projection based on Actual Data through FY 2000

# Fee-Paying Full Application Equivalents

Using 1993-2000 Data, Adjusted for PDUFA II Rules



BILLING CODE 4160-01-C

Attachment I

PDUFA II Five Year Plan—2001 Update

The total FY 2001 application fee revenue is estimated by multiplying the adjusted application fee rate (\$309,647) by the equivalent number of applications projected to qualify for fees in FY 2001 (163.6), for a total estimated application fee revenue in FY 2001 of \$50,658,249. This is the amount of revenue that FDA is also expected to derive both from establishment fees and from product fees.

#### IV. Adjustment for Excess Collections in Previous Years

Under the provisions of the PDUFA II, if the agency collects more fees than were provided for in appropriations in any year after 1997, FDA is required to reduce its anticipated fee collections in a subsequent year by that amount (21 U.S.C. 379h(g)(4)).

In FY 1998, Congress appropriated a total of \$117,122,000 to FDA in the PDUFA II fee revenue. To date, collections for FY 1998 total \$117,446,776—a total of \$324,776 in excess of the appropriation limit. This is the only fiscal year since 1997 in which FDA has collected more in the PDUFA II fees than Congress appropriated.

FDA also has requests for waivers or reductions of FY 1998 fees pending that,

if granted, would eliminate the excess collections. For this reason FDA is not reducing its FY 2001 fees to offset excess collections at this time. An offset will be considered next year, when fees for FY 2002 are established, if FDA still has collections in excess of appropriations for FY 1998 after the pending requests for FY 1998 waivers and reductions have been resolved.

#### V. Fee Calculations for Establishment and Product Fees

##### A. Establishment Fees

At the beginning of FY 2000, the establishment fee was based on an estimate of 318 establishments subject to fees. For FY 2000, 372 establishments qualified for and were billed for establishment fees, before all decisions on requests for waivers or reductions were made. FDA estimates that a total of 25 establishment fee waivers or reductions will be made in FY 2000, for a net of 347 fee-paying establishments, and will use this number for its FY 2001 estimate of establishments paying fees, after taking waivers and reductions into account. The fee per establishment is determined by dividing the adjusted total fee revenue to be derived from

establishments (\$50,658,249), by the estimated 347 establishments, for an establishment fee rate for FY 2001 of \$145,989 (rounded to the nearest dollar).

##### B. Product Fees

At the beginning of FY 2000, the product fee was based on an estimate that 2,262 products would be subject to product fees. By the end of FY 2000, 2,369 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 and reductions made, FDA estimates that 2,314 products will qualify for product fees in FY 2000, after allowing for waivers and reductions, and will use this number for its FY 2001 estimate. Accordingly, the FY 2001 product fee rate is determined by dividing the adjusted total fee revenue to be derived from product fees (\$50,658,249) by the estimated 2,314 products for a product fee rate of \$21,892 (rounded to the nearest dollar).

#### VI. Adjusted Fee Schedule for FY 2001

The fee rates for FY 2001 are set out in table 2 of this document:

TABLE 2.

Fee Category	Fee Rates for FY 2001
Applications	
Requiring clinical data	\$309,647
Not requiring clinical data	\$154,823
Supplements requiring clinical data	\$154,823
Establishments	\$145,989
Products	\$21,892

#### VII. Implementation of Adjusted Fee Schedule

##### A. Application Fees

Any application or supplement subject to fees under the PDUFA II that is submitted after December 31, 2000, must be accompanied by the appropriate application fee established in the new fee schedule. Payment must be made in U.S. currency by check, bank draft, or U.S. postal money order payable to the order of the 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, the courier can deliver the checks to: Food and Drug Administration (360909) Mellon Client Service Center rm. 670, 500 Ross St., Pittsburgh, PA 15262-

0001. (Note: This is a new Mellon Bank Address for courier delivery only.)

Please make sure that the FDA P.O. Box number (PO Box 360909) is on the enclosed check.

FDA will bill applicants who submitted lower application fees from October 1 to December 31, 2000, for the difference between the amount they submitted and the amount specified in the Adjusted Fee Schedule for FY 2001.

##### B. Establishment and Product Fees

By December 31, 2000, FDA will issue invoices for establishment and product fees for FY 2001 under the new Adjusted Fee Schedule. Payment will be due by January 31, 2001. FDA will issue invoices in October 2001 for any products and establishments subject to fees for FY 2001 that qualify for fees after the December 2000 billing.

Dated: December 7, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00-31949 Filed 12-15-00; 8:45 am]

BILLING CODE 4160-01-F

#### DEPARTMENT OF HEALTH AND HUMAN SERVICES

##### Food and Drug Administration

[Docket No. 00D-1632]

**International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH); Draft Guidance on "Pharmacovigilance of Veterinary Medicinal Products: Management of Adverse Event Reports (AER's)" (VICH GL24); Availability; Request for Comments**

AGENCY: Food and Drug Administration, HHS.

# PDUFA II Fee and Revenue Estimation Worksheet

## FY 2001 Updated Estimate

Actual Amounts Collected as of 9/30/00 shown for FY 1998, FY 1999 and FY 2000

Forecast for 2001 and 2002 based Regression Analysis Trendline of Submissions from FY 1993 through FY 2000

Fiscal Year	1998 Actual <sup>3</sup>	1999 Actual <sup>3</sup>	2000 Actual <sup>3</sup>	2001 Estimate	2002 Estimate
Statutory Full Application Fee	\$250,704	\$256,338	\$256,338	\$267,606	\$258,451
Cumulative Inflation Percentage since 1997 <sup>1</sup>	2.45%	6.22%	11.47%	15.71%	20.00%
Fee per Full Application, after Inflation	\$256,846	\$272,282	\$285,740	\$309,647	\$310,130
Estimated Equivalent of Full Applications <sup>2</sup>	119	151	153.5	163.6	171
<b>Est. Total Application Fee Revenue</b> After Accounting for Waivers	<b>\$30,493,387</b>	<b>\$38,636,530</b>	<b>\$48,066,442</b>	<b>\$50,658,249</b>	<b>\$53,032,278</b>
<b>Est. Total Product Fee Revenue</b>	<b>\$41,513,476</b>	<b>\$41,833,192</b>	<b>\$43,829,964</b>	<b>\$50,658,249</b>	<b>\$53,032,278</b>
Estimated # of Products	2225	2134	2262	2314	2314
Product Fee	\$18,459	\$18,364	\$19,959	\$21,892	\$22,918
<b>Est. Total Establishment Fee Revenue</b>	<b>\$45,439,914</b>	<b>\$41,541,794</b>	<b>\$45,802,541</b>	<b>\$50,658,249</b>	<b>\$53,032,278</b>
Estimated # of Establishments	320	315	318	347	347
Establishment Fee	\$141,966	\$128,435	\$137,928	\$145,989	\$152,831
<b>Estimate of Total Revenue</b>	<b>\$117,122,000 <sup>4</sup></b>	<b>\$122,011,516</b>	<b>\$137,698,947</b>	<b>\$149,273,000 <sup>5</sup></b>	<b>\$159,096,835</b>
<b>Five-Year Total:</b>					<b>\$685,202,298</b>

<sup>1</sup> Based on increases of 2.45% in 1998, 3.68% in 1999, 4.94% in 2000, 3.81% in 2001, and estimated at 3.7% for FY 2002.

<sup>2</sup> Number after allowing for Exemptions and Waivers--FY 2001 and FY 2002 Estimates Based on Latest Trendline.

<sup>3</sup> Actual Figures are as of 9/30/1999 and will be adjusted by both accounts receivable collected and waivers granted.

<sup>4</sup> Actual Total for FY 1998 is \$117,446,776. The amount shown as the total is the amount appropriated from fees in FY 1998. Fees collected in excess of \$117,122,000, after all appeals and waivers are decided, will be used to offset collections in a later year.

<sup>5</sup> The President's FY 2001 Budget estimates \$149,273,000 million; but data available after that budget was submitted indicate that about a higher amount will be collected in FY 2001. A supplemental budget request supporting this larger amount is under discussion.

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

**FY 2001**

**April 2001**

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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;
- new goals for responding to industry requests for meetings, documenting outcomes of those meetings and for handling dispute resolutions; and
- 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. In addition, the development of infrastructure to provide the tools necessary to move to electronic application receipt and review 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. It reflects a project-oriented view of the ERSR program 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. 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 PDUFA II Information Management Five-Year Plan (FY 2001) is organized as follows:

- Section 2.0 describes the PDUFA II goals supported by the establishment and implementation of the ERSR Program;
- 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 program oversight processes for the ERSR program; and
- Section 6.0 provides a summary of the ERSR Program.
- Appendix A: ERSR Program Budget
- Appendix B: Glossary of Acronyms

## **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 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, archival, and tracking of electronic submissions. While PDUFA II specifies INDs and human drug applications, CBER and CDER are planning to accommodate additional application types.

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.

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 II 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 problems<sup>1</sup>. 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.

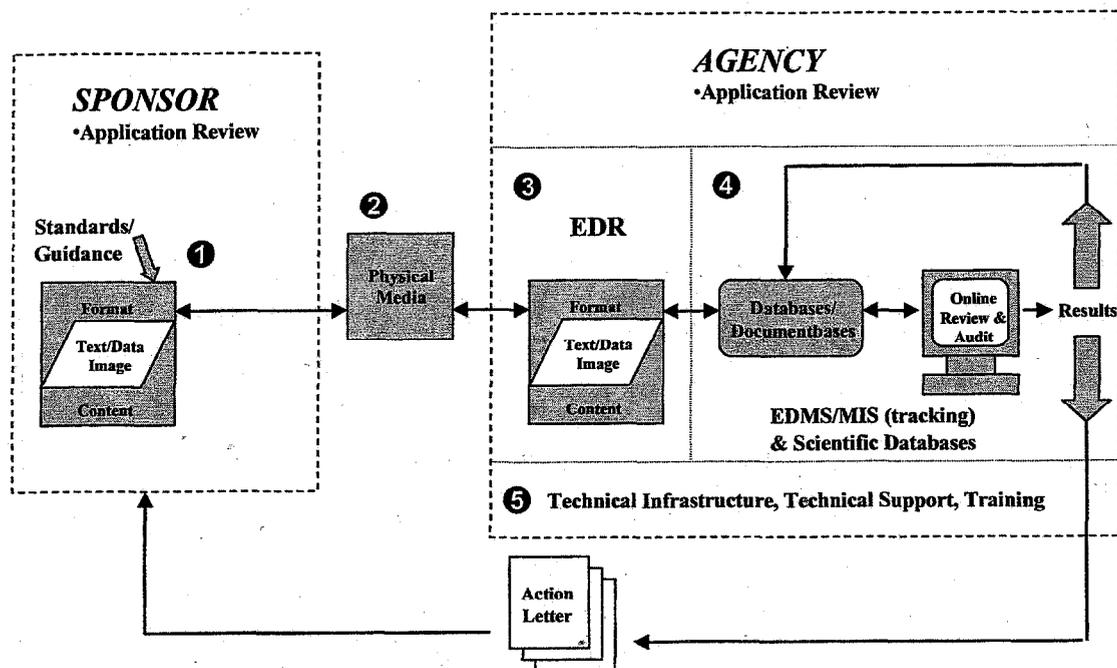


Figure 1

***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 submission guidance (1)***

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

<sup>1</sup> 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.

as the foundation for enabling regulated industry to exchange electronic submissions with the Agency.

*Physical Media (2)*

Electronic submissions that conform to the established standards and industry guidance are submitted via a defined storage format.<sup>2</sup>

*Design and implement systems (3,4)*

There are various systems required to provide the capability and capacity for receiving, reviewing, archiving, and tracking submissions electronically. An electronic document room accommodates the receipt, archive, and storage of these submissions. Management information systems enable reviewers 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. Electronic document management systems provide capability to store, route, and retrieve at a later date.

*Update the technical and non-technical infrastructure (5)*

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 a secure e-mail package for communicating with regulated industry, capability for field component 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 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.

---

<sup>2</sup> The development of an electronic Gateway for the transmission of electronic submissions was evaluated but not selected for implementation. Electronic submissions will be received in a defined format and saved to CD ROMs.

## **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 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.

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.

The activities within the ERSR program are influenced most by the ICH M2 Expert Working Group (EWG) 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 maintains a series of recommendations for facilitating electronic communications, including recommendations for physical media, networking, secure EDI transmission over the Internet, and electronic document format. FDA is also active in the ICH M4 EWG, which focuses on the Common Technical Document (CTD) for the technical content of sections of the NDA. The electronic CTD work is planned for completion by the end of FY2001.

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.

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 standardizes the information systems architecture of the entire Agency beginning with the e-mail system, the network operating system, and the desktop operating system. The ISA decreases operations and maintenance costs and decreases training time and costs by providing users with a common environment for basic computing needs.

## 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. In January 1999, the FDA published *Guidance for Industry: Providing Regulatory Submissions in Electronic Format - General Considerations* and *Guidance for Industry: Providing Regulatory Submissions in Electronic Format - NDAs*. These guidance documents provide for the receipt and archive of full electronic NDAs without an accompanying paper archival copy.

An important challenge affecting guidance for and the receipt and archive of submissions 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.<sup>3</sup>

CBER published guidance in November 1999 for electronic submission to CBER of a Biologics License Application (BLA), Product License Application (PLA)/Establishment License Application (ELA) and New Drug Applications (NDAs).

Guidance documents and target dates for publishing additional documents are provided below<sup>4</sup>:

February 2001	(CDER & CBER) Publish joint guidance document for advertising and promotional labeling.
August 2001	(CBER) Develop and publish guidance to define general considerations for secure electronic mail pilot.
September 2001	(CDER & CBER) Publish joint guidance document for the electronic submission of Investigational New Drug (IND) Applications.
December 2001	(CBER) Develop and issue guidance to industry that defines electronic submission guidelines for Pre-market approval (PMAs) and premarket notification (510Ks).
September 2002	(CDER & CBER) Develop and publish guidance documents for the electronic submission of Drug Master Files (DMFs) and Annual Reports.

The chart on the following page shows the schedule for these guidance activities.

<sup>3</sup> Policy regarding Part 11 will be coordinated through the Office of Regulatory Affairs. That policy will be executed through the development of IT systems within the ERSR project.

<sup>4</sup> Note: Accomplishments from prior periods are reflected in the Project Plan Gantt Charts.



### 4.3 Design and Implement Systems

*ERSR Subgoal: Design and implement systems to provide the capability and capacity for the receipt, review, archive 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, archive, and track submissions electronically. Electronic submissions that conform to the established standards and industry guidance are transmitted via acceptable physical media to an Electronic Document Room. Systems have been developed to provide an automated means for creating, managing, and archiving internally generated review documents. Other systems track the status and progress of submissions submitted to the Agency for action, generate mandatory user fee reports, and enable tracking of milestones and workload statistics for improved management accountability. In addition, there are many design and implementation activities being conducted regarding scientific databases (also known as structured databases) needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop.

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

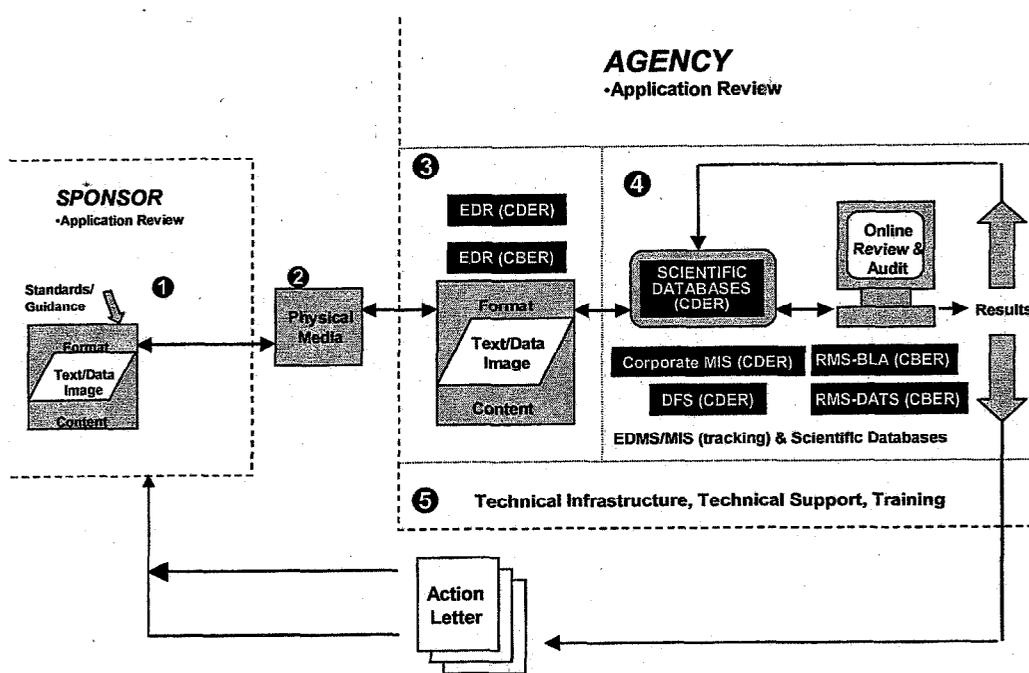


Figure 2

CDER Electronic Document Room (EDR)

CDER currently provides the capability to receive, archive, and store full electronic New Drug Applications (NDAs). Ultimately, CDER's EDR will also accommodate 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 electronic Case Report Forms (CRFs) and Case Report Tabulations (CRTs) for NDAs without an accompanying paper copy. In FY 1999, the EDR was expanded to accommodate full electronic NDAs. Approximately 51% of original NDAs received in CDER in FY 2000 include sections that conform to the electronic submission guidance. From January 1999 to September 1999, CDER received 36 original NDAs that included electronic components and nine NDAs that were fully electronic. From October 1999 to September 2000, CDER received 66 original NDAs that included electronic components. In the first quarter of FY 2001 26 of 33 (78.8%) original NDAs have been submitted with sections conforming to the electronic submission guidance. Of these 50% were total electronic submissions without paper.

CDER's targeted activities are the following:

4 <sup>th</sup> quarter FY 2001	CDER plans to have expanded the capability and capacity of the EDR to accommodate INDs.
4 <sup>th</sup> quarter FY 2002	CDER expects to accommodate DMFs, and Annual Reports by the end of September 2002.

CDER Scientific Databases

Scientific Databases/Informatics (also known as structured databases) are needed by reviewers to perform standard analytical processes on electronic submissions directly from the desktop. CDER is developing carcinogenicity and reproductive/developmental toxicity databases and search tools 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.

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 <sup>th</sup> quarter FY 2001	CDER expects to complete the assembly of the drug-drug interaction data in a unified database to facilitate retrieval and analysis by September 2000.
4 <sup>th</sup> 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. Work on this task continues to progress at a satisfactory rate. The current focus is to provide mechanisms for capturing information automatically from electronic submissions, developing datamining and modeling tools and for integrating toxicology information into the electronic review environment.

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 reviews on-line from their desktops rather than relying on paper copies.

During FY 1999, CDER completed deployment of DFS to all new drug review divisions throughout the Center. As of October 1999, approximately 47,000 review documents had been checked into DFS.

By the close of FY 2000, CDER successfully deployed DFS v2.0 to all CDER reviewers. DFS v2.0 was 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. With the release of DFS v2.0, the Center Director mandated that all Center Reviewers use the system for all internally generated review documents. CDER expects that DFS will reduce costs by eliminating the need for document room personnel to reproduce and distribute final form copies.

Also, by the end of FY 2000, CDER had successfully deployed the first phase of its Electronic Document Query (E-Doc Query) system. The E-Doc Query project involved replacing the former search and retrieval system -- Excalibur's Electronic Filing System (EFS) -- with RetrievalWare. The ultimate goal of this project was to provide query and retrieval capability of the electronic document images and text stored in EFS in several different repositories. The E-Doc Query System will provide a single, integrated query solution that encompasses all of CDER's centrally maintained electronic data and documents.

Targeted activities for CDER's DFS are:

4 <sup>th</sup> quarter FY 2002	CDER will continue to operate and maintain the Division Files System (DFS)
4 <sup>th</sup> quarter FY 2002	CDER intends to expand the capability of the E-DOC Query System to incorporate access to additional document repositories and to provide additional, specific querying functions.

#### Corporate Database Redesign

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 Corporate 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 of 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 Corporate Database. The integrity and quality of this 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 in the process of redesigning its Corporate Database to develop a modern, flexible, and comprehensive database structure on which to base future applications development.

During FY 1999, CDER completed the definition of data and functional requirements to meet the needs of FDAMA, PDUFA II, ERSR and other critical tracking and review activities. CDER also developed a logical

data model for the redesigned Corporate Database and initiated and issued a contract for migration of legacy data.

In FY 2000, CDER gathered and documented the data requirements and associated functional requirements for the Corporate Database Redesign project.

Targeted activities for CDER's Corporate MIS are:

3 <sup>rd</sup> quarter FY 2002	CDER plans to have completed all software development required for this project.
3 <sup>rd</sup> quarter FY2002	CDER expects to have completed the mapping of existing COMIS data to the new database structure. Additionally, CDER plans to have developed a strategy for migrating data to the new structure and to have completed actual data migration.

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



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.

Effective July 2000, CBER implemented Phase I of the EDR which established the basic infrastructure for the EDR to include hardware and software architecture, security controls and some functionality to support the receipt and reviewing of electronic BLAs, INDs and to process CBER Internal Documents associated with electronic BLAs. Additionally, CBER has since completed Phase II of their EDR that provides the capability to receive additional Internal Final Documents and integrated the EDR with RMS-BLA, DATS, and BIMS.

Targeted activities for CBER's EDR are:

- |                                 |  |
|---------------------------------|--|
| 4 <sup>th</sup> quarter FY 2001 | CBER plans to have completed Phase III of the EDR and will have the ability to send and receive secure e-mail within its pilot program.                      |
| 4 <sup>th</sup> quarter FY 2002 | CBER plans to have completed Phase IV of the EDR. This final phase will provide the capability to receive and archive and review 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 and enforcing review timelines established under PDUFA. The Biologics License Application (BLA) component of RMS incorporates new business rules (21CFR601) and requirements of PDUFA II and replaces the legacy Biologics Regulatory Management System (BRMS). The component for managing Lot Release (RMS-LRS) interfaces with RMS-BLA and replaces a legacy Lot Release System. The Document and Accountability and Tracking System component (RMS-DATS) also interfaces with RMS-BLA. RMS-BLA presently has a limited interface with CBER's legacy Biologics IND Management System (BIMS) system. Enhancements are planned for the BIMS to provide better interfaces between data in the BIMS and RMS-BLA databases.

Effective July 2000, CBER completed Phase I of the RMS-BLA module that provides CBER the functionality to process therapeutic, vaccine, allergenic, and blood product BLA submissions. CBER completed data migration from the legacy BRMS system for initial operational capability. RMS-LRS was also put into production with an interface to RMS-BLA in July 2000.

Targeted activities for CBER's RMS are:

- |                                 |   |
|---------------------------------|---|
| 3 <sup>rd</sup> quarter FY 2001 | Populate (through migration and manual data entry) additional product information from legacy BRMS and from paper source. Add functionality for additional reporting capability and for better management of BLA submissions that affect multiple products. |
| 4 <sup>th</sup> quarter FY 2001 | CBER will have completed the enhancement of the RMS-BLA module, and most of the remaining data migration.   |

1 <sup>st</sup> quarter FY 2002	CBER expects to have greater integration with the BIMS and EDR
4 <sup>th</sup> quarter FY 2002	CBER will have completed Phase II (the balance of the data migration) of RMS. With completion of this phase, CBER will be able to track all applications.

*CBER Document Accountability and Tracking System (RMS/DATS)*

CBER developed DATS to consolidate administrative document logging and circulation control activities by replacing two legacy systems. While it is planned to have information from DATS 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 also provides the capability to enter key information from FDA Forms 1571 and 356h that are submitted to CBER by sponsors and applicants as part of IND and BLA submission, respectively. Upon the rollout of RMS-BLA, DATS was interfaced with the RMS-BLA becoming one of the components of RMS (RMS-DATS).

The Phase II of DATS with release 3.0 was completed in July 2000. Phase II provides the capability to track routing and circulation information and is interfaced with RMS/BLA.

3 <sup>rd</sup> quarter FY 2001	Complete development of the process to track and route IND communications previously managed by the legacy Biologics IND Management System (BIMS).
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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 activities support multiple projects and are coordinated with projects' functionality, as appropriate. Infrastructure includes 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. 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 ERSR project members had considered utilizing an Electronic Gateway to receive submissions directly but this framework was not selected due to concerns of security, reliability and overall efficiency—from both an industry and Center perspective. As technology advances, an electronic Gateway may be reconsidered but for the foreseeable future, the approach for submission, as indicated in the guidance documentation, is the use storage of data to CD ROM diskettes.

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.

Accomplishments to date have included upgrading desktops within the Center to the ISA-standard desktop configuration (Windows 95, Office 97, Outlook 97), and migrating the network infrastructure to ISA standards (BackOffice 4.5, CAT 5 cabling).

During FY 2000, the Center-wide email upgrade to Outlook 2000 was completed. Installation was completed for the Pilot of Dual Monitor configuration for 40 users. The installation of dark fiber between the CBER's buildings completed the upgrade of networking capability.

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

4 <sup>th</sup> quarter FY 2001	Upgrade desktop hardware and software (MS Office 2000). Additional 40 users added to Pilot for Dual Monitor configuration.
4 <sup>th</sup> quarter FY 2001	CBER will implement a secure messaging pilot capability between Agency Center/Offices and the regulated industry.
On-going activities	Continue providing operations and maintenance support for the technical infrastructure.

*Center for Drug Evaluation and Research (CDER)*

CDER is conducting several activities related to updating its technical infrastructure. One of these activities involves CDER's Enterprise Computing Architecture (ECA) which reflects the current business processes, information flows, applications, data, and technical infrastructure of CDER. The ECA provides CDER with an enterprise-wide conceptual framework for planning the migration to a paperless review environment. Another is updating its current cluster infrastructure.

During FY 2000, CDER continued the secure e-mail project and its PC refreshment program, and initiated a pilot desktop replacement with laptop program for 30 reviewers. Additionally CDER completed several reengineering projects and policy documents related to IT services (e.g., procurement, managed desktop services).

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

On-going activities	Maintain the ECA Description document, incorporating changes to the computing architecture. Additionally, CDER will continue developing, documenting, and maintaining policies and procedures for use when developing and modifying 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 compliance officers in the field offices will need to access documents electronically. ORA envisions that they will need the capability to provide each district office, each laboratory, some large resident posts on the network, and each regional office access to the electronic documents maintained by CDER. ORA will also need to provide the ability to browse and search for the documents pre-authorized for viewing by ORA investigators and compliance officers. ORA does not require detailed access to CBERS BLA applications. As CDER's EDR and DFS systems have reached their maturity, CDER and ORA are now in the position to determine the necessary infrastructure to permit ORA field personnel to access the required documents electronically. This process was initiated in the 2<sup>nd</sup> quarter of FY2001.

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

1 <sup>st</sup> quarter FY2001	Provide detailed requirements to CDER.
2 <sup>nd</sup> quarter FY2001	(With CDER) Complete pilot test to determine the best information access

3 <sup>rd</sup> quarter FY2001	methodology for ORA field personnel.
4 <sup>th</sup> quarter FY2001	Design the infrastructure architecture and complete implementation plan.
4 <sup>th</sup> quarter FY2002	Complete procurement and begin implementation. Complete implementation of infrastructure to electronically access CDER documents.

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 2001)*  
*April 2001*

ID	Task Name	Finish	1998				1999				2000				2001				2002			
			Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
1	CBER	Fri 9/28/01																				
2	Upgrade desktops to ISA-standard desktop configuration	Thu 9/30/99								◆ 9/30												
3	Migrate network infrastructure to ISA standards	Thu 9/30/99								◆ 9/30												
4	Certify mission critical systems are Y2K compliant	Sat 1/1/00								◆ 1/1												
5	Complete installation of dark fiber between CBER component offices	Sat 9/30/00												◆ 9/30								
6	Implement a secure e-mail solution	Fri 9/28/01																				◆ 9/28
7	CDER	Sun 9/1/02																				
8	Define and document requirements for secure electronic mail	Tue 9/1/98	◆ 9/1																			
9	Conduct a secure e-mail pilot	Tue 6/1/99								◆ 6/1												
10	Publish draft Enterprise Computing Architecture Description document	Tue 9/1/98	◆ 9/1																			
11	Conduct Y2k testing and IV&V of mission critical systems	Wed 3/31/99																				
12	Certify mission critical systems are Y2K compliant	Wed 3/31/99								◆ 3/31												
13	Continue developing ECA description document	Sun 9/1/02																				
14	Continue upgrading desktops and network operations to ISA standard configurations	Thu 9/30/99																				
15	Replace obsolete disk drives, upgrade network, upgrade desktop SW/HW, replace LAN printers	Thu 12/10/98																				
16	ORA	Mon 9/30/02																				
17	Complete ORA's functional requirements analysis	Fri 12/29/00												◆ 12/29								
18	Pilot Test	Fri 3/30/01																				
19	Design architecture and Implementation Plan	Mon 6/4/01																				◆ 6/4
20	Complete Procurement	Thu 12/27/01																				◆ 9/28
21	Implementation	Mon 9/30/02																				
22	OIRM	Mon 7/1/02																				
23	Complete oversight of renovation, testing, and IV&V of mission critical systems	Fri 5/14/99								◆ 5/14												
24	Publish Annual Plan	Mon 6/3/02	◆ 6/1							◆ 6/1				◆ 6/1								◆ 6/3
30	Collect performance information	Mon 7/1/02								◆ 7/1	◆ 1/3		◆ 7/3	◆ 1/2	◆ 7/2	◆ 1/2		◆ 7/1				
38	Conduct annual independent review of ERSR Program	Mon 6/3/02								◆ 6/2				◆ 6/2								◆ 6/3

## **5.0 OVERALL PROGRAM OVERSIGHT**

The FDA CIO is responsible for ensuring that PDUFA II IT investments fit into a common computing environment and follow current IT management practices. 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 FDA's IT Business Planning (ITBP) process, as Re-engineered during FY 2000, is utilized to review existing ERSR IT projects. This process is consistent with Department of Health and Human Services (DHHS) policies and recent legislation, including the Clinger-Cohen Act and is applied to all FDA IT investments. It is the goal of the CIO to promote Center progress towards Level 2 of the Capability Maturity Model for IT project planning and management as a model for other ERSR components and throughout the Agency.

An integral part of the FDA business planning process is the review of 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).

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, compliance with Agency IT security standards 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.

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 is a means of communicating the progress and status of the ERSR Program to both internal and external parties. Additionally, information about ERSR issues and activities is shared with industry through the Information Management Advisory Board (IMAB). This Board is comprised of both Agency management and industry representatives. The Board functions as a steering committee that ensures the PDUFA II Information Management Plan reflects the interest of all stakeholders and utilizes information management/technology best practices, and that the PDUFA II information management program implementation is consistent with that plan. The IMAB provides a forum for any issues or questions not addressed by this plan. Specific issues raised at the IMAB can then be channeled to the appropriate Agency organization.

The Office of the CIO (OCIO) reviews the major project activities within the ERSR project. The CIO plays the following roles as part of the ERSR project:

- Facilitates coordination of IT capital planning;
- Reviews progress and promotes integration of major IT projects, when feasible;
- Ensures compliance with FDA technology and security standards; and
- Oversees development and coordination of contingency plans and resources, when feasible.

In FY2000, the OCIO implemented re-engineered IT business processes to support PDUFA oversight. Additionally, through FY2002, the OCIO will coordinate development and implementation of IT security policies necessary for ERSR and all other FDA IT investments.

In order to provide project management coordination, the OCIO is investing resources in consulting support. Additionally, OCIO is piloting an internal intranet-based data repository and reporting tool to enhance project planning coordination among the Centers and the OCIO and reduce the reporting burden of IT project management.

The targeted activities for the CIO oversight function are:

FY 2001	Develop and implement IT project management plans including OIRM Action Plan and project management training.
Through 2002	Develop security policies and plans.

## **6.0 SUMMARY**

The overall PDUFA goal of developing and updating the information management infrastructure to allow, by fiscal year 2002, the paperless receipt and processing of INDs and human drug applications is composed of four subgoals:

- developing standards;
- issuing guidance for regulated industry for electronic submissions;
- designing and implementing systems for receiving, reviewing, archiving 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. To help ensure coordination of all ERSR related activities, the CIO will coordinate an internal forum of key participants to review current project status and forecast the operational impact of the final integrated project.

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 to meet their unique regulatory review requirements, and these processes dictate their systems 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.

Significant effort was expended in FY 1999 across the Agency toward ensuring that systems and infrastructure (both PDUFA and non-PDUFA related) were not vulnerable to the Year 2000 (Y2K) date change. FDA engaged in an intensive effort that 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 was the impact of the Y2K issue on its mission-critical functions. Consequently, all efforts were prioritized to ensure neither the Agency nor the public was 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. PDUFA-related (i.e., pre-market) components within these systems were given the highest priority to meet the overall PDUFA IT goal of having an ability to receive and process submissions electronically by FY 2002.

During FY 2000, the focus of the ERSR IT program was again upon systems development in support of the overall goal. Significant progress was made in all areas towards achieving a paperless ERSR environment.

CDER published guidance for the submission of three types of licensing applications and for new drug applications. Phase I and Phase II of the CDER Electronic Document Room was completed, establishing the basic infrastructure for the EDR and allowing limited electronic document exchange. Phase I of the CDER Regulatory Management System was completed to allow processing of Biologics License Applications. Phase II of CDER's Document Accountability and Tracking System was completed providing capability to track routing and circulation information and is interfaced with RMS/BLA.

CDER began receiving original new drug applications with electronic components and an increasing number are completely paperless. The electronic division files system is being used by all Center Reviewers for internally generated review documents. The first phase of CDER's Electronic Document Query System was successfully deployed, replacing Excaliber's Electronic Filing System with RetrievalWare. Infrastructure upgrades improved CDER and CDER's ability to operate in a paperless environment.

Progress was made in defining the requirements for updating the technical and non-technical architecture to allow for electronic access by ORA field personnel. It is expected that these requirements will be finalized in the early part of FY 2001 and tangible results will be seen in FY 2001.

The goal of having the ability to receive and process submissions electronically by FY 2002 is achievable. Steady progress is being made as subgoals are attained by all FDA organizations.

**APPENDIX A**  
**ERSR PROGRAM BUDGET**

**ERSR Program Budget**  
 (in thousands)

<b>CBER</b>	<b>FY1998 Actual</b>	<b>FY1999 Actual</b>	<b>FY2000 Actual</b>	<b>FY2001 Plan</b>	<b>FY2002 Plan</b>	<b>Total Planned</b>
<b>Standards</b>	50	125	0	0	0	175
<b>EDR</b>	407	2,106	1,331	1,050	1,050	5,944
<b>RMS</b>	3,100	2,261	3,322	3,900	3,880	16,463
<b>Other Information Doc Mgt Systems</b>	859	1,148	603	463	359	3,432
<b>Technical Infrastructure</b>	1,642	1,863	947	927	927	6,306
<b>Expenditures by OCIO</b>	0	0	180	167	170	516
<b>CBER Subtotal</b>	<b>6,058</b>	<b>7,503</b>	<b>6,383</b>	<b>6,507</b>	<b>6,386</b>	<b>32,836</b>

<b>CDER</b>	<b>FY1998 Actual</b>	<b>FY1999 Actual</b>	<b>FY2000 Actual</b>	<b>FY2001 Plan</b>	<b>FY2002 Plan</b>	<b>Total Planned</b>
<b>Standards</b>	130	133	3	160	160	586
<b>EDR</b>	401	906	574	411	290	2,582
<b>Scientific Databases</b>	90	353	75	322	250	1,090
<b>EDMS/DFS</b>	2,339	2,455	3,068	775	1,725	10,362
<b>Corporate MIS</b>	773	2,664	2,243	224	2,175	8,079
<b>Other Initiatives</b>	3,785	4,197	5,345	7,468	5,594	26,389
<b>Expenditures by OCIO</b>	0	0	1,861	338	344	2,544
<b>CDER Subtotal</b>	<b>7,518</b>	<b>10,708</b>	<b>13,169</b>	<b>9,698</b>	<b>10,538</b>	<b>51,631</b>

**ERSR Program Budget, continued**  
 (in thousands)

<b>ORA</b>	<b>FY1998 Actual</b>	<b>FY1999 Actual</b>	<b>FY2000 Actual</b>	<b>FY2001 Plan</b>	<b>FY2002 Plan</b>	<b>Total Planned</b>
<b>Electronic Submissions</b>	165	80	0	0	0	80
<b>Document Management</b>	0	0	0	50	260	310
<b>Field Office Electronic Review</b>	347	0	64	823	711	1,945
<b>ORA Subtotal</b>	<b>512</b>	<b>80</b>	<b>64</b>	<b>873</b>	<b>971</b>	<b>2,500</b>

<b>CENTER TOTALS</b>	<b>FY1998 Actual</b>	<b>FY1999 Actual</b>	<b>FY2000 Actual</b>	<b>FY2001 Plan</b>	<b>FY2002 Plan</b>	<b>Total Planned</b>
<b>CBER</b>	6,058	7,503	6,383	6,507	6,386	32,836
<b>CDER</b>	7,518	10,708	13,169	9,697	10,538	51,631
<b>ORA</b>	512	80	64	873	971	2,500
<b>Center Total</b>	<b>14,088</b>	<b>18,291</b>	<b>19,616</b>	<b>17,077</b>	<b>17,895</b>	<b>86,967</b>

**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)
M4	ICH M4 EWG focuses on Common Technical Documents (CTD)
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