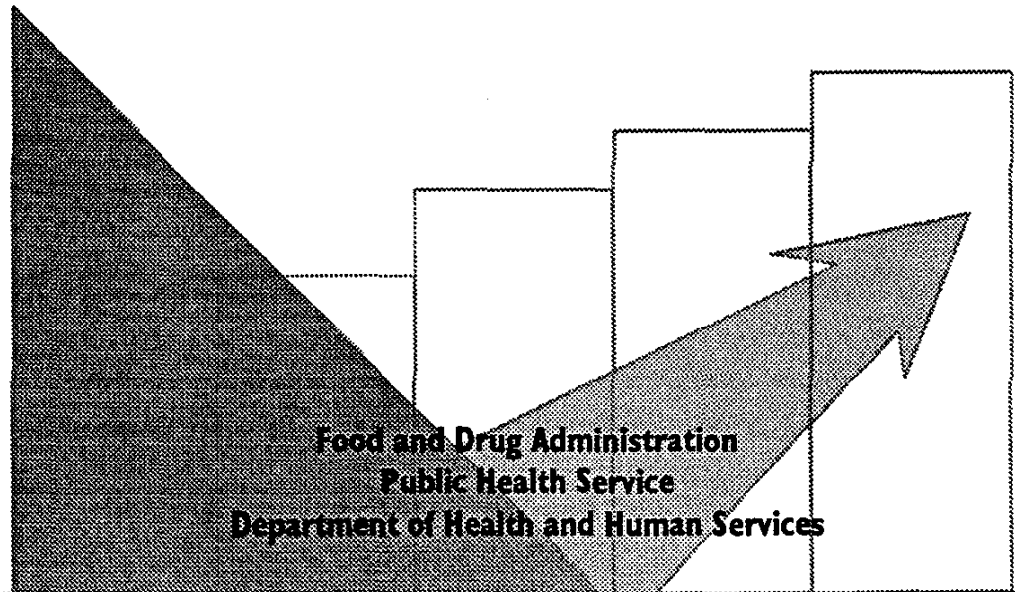


# **THIRD ANNUAL FINANCIAL REPORT**

## **Prescription Drug User Fee Act of 1992**

**Fiscal Year 1995 Report to Congress**

*February 1, 1996*



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## BACKGROUND

The Prescription Drug User Fee Act of 1992 ("PDUFA", "User Fee Act", or "Act") authorizes the Food and Drug Administration ("FDA" or "Agency") to collect fees from the prescription drug industry to augment FDA's base resources. These additional resources are to be used to expedite the review of human drug applications, so that prescription drug products can reach the marketplace more quickly. Total fee revenues that FDA is to collect in each fiscal year (FY) are set in the Act. These amounts are to be adjusted for FYs 1994 through 1997 to reflect the greater of increases in the Consumer Price Index or the rate of pay increases to federal employees in the Washington, D.C., area. Application, establishment, and product fees set out in a schedule in the Act are to be adjusted on an annual basis to achieve the revenue targets set forth in the Act.

Section 104 of the Act requires FDA to submit two reports to Congress each year. They are a performance report and a financial report due within 60 and 120 days of the end of the FY, respectively. The performance report, which discusses FDA's progress in meeting the goals referred to in the Act, was released December, 1995. The financial report addresses FDA's implementation of the authority for the collection and use of user fees during a fiscal year.

This third annual financial report presents the user fee revenues and related obligations for FYs 1993, 1994 and 1995 and the costs applicable to the process for the review of human drug applications at the FDA for the same period. FY 1992 costs for the process for the review of human drug applications have been included and adjusted as specified in the Act, because this amount is a baseline for future year calculations. Arthur Andersen & Company independently reviewed FDA's procedures for calculating these costs in 1995, and found the methodology to be reasonable.

Additionally, in FY 1995, in compliance with the Chief Financial Officers Act requirements, FDA's Office of Financial Management prepared a financial statement which reported the condition and results of the PDUFA account as of and for the year ended September 30, 1994. The Office of the Inspector General (OIG) audited this financial statement and issued its audit report on September 25, 1995. The OIG rendered an unqualified opinion on the PDUFA account's statement of operations and changes in net position.

### COMMISSIONER'S REPORT

This Third Annual Report to Congress on the financial aspects of FDA's implementation of the Prescription Drug User Fee Act of 1992 (PDUFA) covers FY 1995, from October 1, 1994, through September 30, 1995. The PDUFA established certain conditions that must be satisfied each year in order for FDA both to collect the user fees established in the Act and to spend those revenues to enhance FDA's process for the review of human drug and biological product applications. This report documents how those statutory conditions were met in FY 1995. Since the conditions were met, FDA both collected and spent PDUFA user fees in FY 1995.

The FY 1992 financial information is established by PDUFA as a baseline year and will be adjusted for inflation, as required by the Act, and presented in financial reports each year for comparison. The statements and tables included in this report provide information on the user fees FDA collected and spent in FY 1995, and also provide comparative data for FYs 1994, 1993, and baseline cost data for 1992. Over the past three years, FDA has collected over \$150 million in user fees of which \$123 million has been obligated and spent.

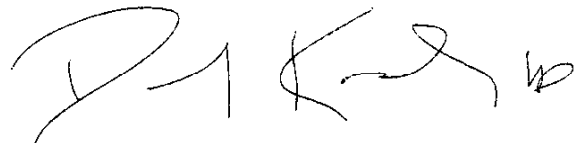
In FY 1995, FDA collected \$70,953,500 in user fees and had gross receivables of \$1,608,500. In addition, at year end, the Agency had a substantial number of reviews in process for applications received in FY 1995 (and a few received in 1994 and 1993), for which the second half of the application fee will not be billed until FDA issues an action letter on the application. Most of these action letters will be issued, and fees collected, in FY 1996; some may not be issued until FY 1997 or beyond.

In FY 1995, FDA obligated and spent \$74,064,015 of fees collected this year or carried over from previous years, of which over 95 percent were for direct review actions. When accounts receivable are included, there remains a total of \$31,860,205 of unobligated fees that are available to the agency for future expenses as of September 30, 1995.

Of the \$74,064,015 that FDA spent in FY 1995, \$33,294,000 was for increased staff and payroll costs. By the end of the year, the level of effort devoted to the process for the review of human drug applications was the equivalent of 453 staff years more than was expended in FY 1992. This large and growing infusion of human resources into the process is one of the most important factors which enabled FDA to continue to meet the performance goals in the Act. The costs for payroll and benefits are expected to increase in FY 1996 as staff increases are expected to continue.

The balance of the fee revenue spent in FY 1995 represents investments in the Agency's infrastructure and other activities supporting the process for the review of human drug applications. These include vital investments in the continued development of information technologies.

We are pleased with our progress in enhancing the review of human drug applications in FY 1995 that has been made possible by the fees we have collected under this Act. We look forward to continued improvements and investments in 1996 that will further strengthen and enhance our human drug application review process.

A handwritten signature in black ink, appearing to read "D. A. Kessler" with a stylized flourish at the end.

David A. Kessler, M.D.  
Commissioner of Food and Drugs

### AUTHORITY FOR USER FEES IN 1995

The Act contains three conditions that must be met in order to implement user fees. These conditions are presented in Appendix A. FDA did meet all necessary criteria in FY 1995.

The first condition is that FDA's Salaries and Expenses Appropriation, excluding user fees, for FY 1995 must exceed FDA's FY 1992 Salaries and Expenses Appropriation, as adjusted for inflation according to the Act. FDA's FY 1995 Salaries and Expenses Appropriation, excluding user fees, was \$817,681,000 after adjustment due to a rescission of \$2,290,000. FDA's FY 1992 Salaries and Expenses Appropriation, after adjusting for inflation, was \$767,690,296. Therefore, the first condition was met.

The second condition is that user fees be provided for in FDA's appropriation. For FY 1995, the basic appropriation act specifying amounts authorized to be collected from fees (Public Law 103-330) was signed by the President September 30, 1994. The appropriation provided funding of \$79,423,000 from PDUFA fees collected to augment FDA's Salaries and Expenses Appropriation. The appropriation act specified that the fees collected could remain available until expended. Thus, the second condition was met.

The third condition in the Act is that all user fees collected under the Act may be used only for increases in the costs of resources allocated for the process for the review of human drug applications, compared with FY 1992 adjusted obligations. The \$139,830,318 obligated from traditional appropriations in FY 1995, exceeded the \$126,958,144 obligated for this purpose in FY 1992, as adjusted. Thus, the third condition has been met. In addition to traditional appropriations, \$74,064,015 of user fees collected were obligated and spent in FY 1995, all for costs related to the process for the review of human drug applications, as required by the Act.

**USER FEE REVENUES AND OBLIGATIONS**

The Act specifies the user fee revenues to be collected from product, establishment, and application fees. Only half of the application fee is due upon submission of an application to the Agency. The remainder of the application fee is due 30 days from the date FDA issues an invoice after issuance of an action letter related to the application. Thus, fee revenue related to submissions received in one year may come due and be collected in succeeding years.

**FOOD AND DRUG ADMINISTRATION  
STATEMENT OF USER FEE REVENUES AND RELATED OBLIGATIONS**

*FOR THE FY ENDED SEPTEMBER 30, 1995*

|                               | <u>FY 1993</u>             | <u>FY 1994</u>             | <u>FY 1995</u>             | <u>TOTAL</u>                |
|-------------------------------|----------------------------|----------------------------|----------------------------|-----------------------------|
| <b>Revenues:</b>              |                            |                            |                            |                             |
| Fees Collected FY 1993        | \$28,531,996               |                            |                            | \$28,531,996                |
| Fees Collected FY 1994        | 5,707,994                  | \$48,022,250               |                            | 53,730,244                  |
| Fees Collected FY 1995        | <u>1,153,500</u>           | <u>6,466,800</u>           | <u>\$63,333,200</u>        | <u>70,953,500</u>           |
| Total Fees Collected          | 35,393,490                 | 54,489,050                 | 63,333,200                 | 153,215,740                 |
| Accounts Receivable           | <u>176,000</u>             | <u>524,900</u>             | <u>907,600</u>             | <u>1,608,500</u>            |
| <b>Total Revenues:</b>        | <b>35,569,490</b>          | <b>55,013,950</b>          | <b>64,240,800</b>          | <b>154,824,240</b>          |
| <b>Obligations:</b>           |                            |                            |                            |                             |
| Fees Obligated FY 1993        | (8,949,000)                |                            |                            | (8,949,000)                 |
| Fees Obligated FY 1994        | (25,290,990)               | (14,660,030)               |                            | (39,951,020)                |
| Fees Obligated FY 1995        | <u>(1,153,500)</u>         | <u>(39,829,020)</u>        | <u>(33,081,495)</u>        | <u>(74,064,015)</u>         |
| <b>Total Obligations:</b>     | <b><u>(35,393,490)</u></b> | <b><u>(54,489,050)</u></b> | <b><u>(33,081,495)</u></b> | <b><u>(122,964,035)</u></b> |
| <b>Balance as of 09/30/95</b> | <b><u>\$176,000</u></b>    | <b><u>\$524,900</u></b>    | <b><u>\$31,159,305</u></b> | <b><u>\$31,860,205</u></b>  |

Total revenues of \$35,569,490 in FY 1993 represent user fees collected or receivable during FYs 1993, 1994, and 1995 related to applications received in 1993. Total revenues of \$55,013,950 in FY 1994 represent user fees collected or receivable during FYs 1994 and 1995 related to applications received in 1994. Total revenues of \$64,240,800 in FY 1995 represent user fees collected or receivable during FY 1995 related to applications received in FY 1995.

User fees are obligated as necessary for the process for the review of human drug applications and unobligated balances continue to be available without FY limitation. Thus, the \$35,393,490 of user fees collected for FY 1993 in FYs 1993, 1994, and 1995 were obligated in FY 1993 (\$8,949,000), FY 1994 (\$25,290,990), and FY 1995 (\$1,153,500). Of the \$54,489,050 of user fees collected for FY 1994 in FYs 1994 and 1995, \$14,660,030 were obligated in FY 1994 and \$39,829,020 were obligated in FY 1995. Of the \$63,333,200 of user fees collected for FY 1995, \$33,081,495 were obligated in FY 1995. The unobligated balance of \$31,860,205 remains available to the Agency for future expenses.

**STATEMENT OF USER FEE REVENUES BY FEE CATEGORY**

|                                  | <u>FY 1993</u>      | <u>FY 1994</u>      | <u>FY 1995</u>      | <u>TOTAL</u>         |
|----------------------------------|---------------------|---------------------|---------------------|----------------------|
| <b>FEEs COLLECTED:</b>           |                     |                     |                     |                      |
| Product Fees                     | \$12,856,000        | \$19,683,600        | \$24,473,200        | \$57,012,800         |
| Establishment Fees               | 11,700,000          | 18,666,200          | 24,768,000          | 55,134,200           |
| Application Fees                 | <u>10,837,490</u>   | <u>16,139,250</u>   | <u>14,092,000</u>   | <u>41,068,740</u>    |
| <b>TOTAL FEES COLLECTED:</b>     | <u>35,393,490</u>   | <u>54,489,050</u>   | <u>63,333,200</u>   | <u>153,215,740</u>   |
| <b>FEEs RECEIVABLE:</b>          |                     |                     |                     |                      |
| Establishment Fees               | 120,000             | 375,200             | 645,000             | 1,140,200            |
| Application Fees                 | <u>50,000</u>       | <u>121,500</u>      | <u>104,000</u>      | <u>275,500</u>       |
| <b>TOTAL FEES RECEIVABLE:</b>    | <u>176,000</u>      | <u>524,900</u>      | <u>907,600</u>      | <u>1,608,500</u>     |
| <b>TOTAL USER FEE REVENUES:</b>  | <u>35,569,490</u>   | <u>55,013,950</u>   | <u>64,240,800</u>   | <u>154,824,240</u>   |
| 1995 User Fees Billed 10&11/95   | 150,000             | 300,600             | 2,992,800           | 3,443,400            |
| Additional Unbilled Fees         | <u>600,000</u>      | <u>2,349,000</u>    | <u>13,884,000</u>   | <u>16,833,000</u>    |
| <b>TOTAL PROJECTED REVENUES:</b> | <u>36,319,490</u>   | <u>57,663,550</u>   | <u>81,117,600</u>   | <u>175,100,640</u>   |
| Appropriations                   | <u>\$36,000,000</u> | <u>\$56,284,000</u> | <u>\$79,423,000</u> | <u>\$171,707,000</u> |

Total fees receivable of \$1,608,500 do not include \$3,443,400 of unbilled 1993, 1994, and 1995 user fees which were billed in October and November 1995.



Additional fees of \$600,000, \$2,349,000, \$13,884,000 related to FYs 1993, 1994, and 1995 submissions, respectively, were not billed or billable as of September 30, 1995, and have not been included in total revenues for FYs 1993, 1994, or 1995. These fees represent application fees to be billed and collected upon completion of the first review action on applications filed in FYs 1993, 1994, and 1995. Therefore, the total projected revenues, before estimated waivers and reductions, related to 1993 submissions are \$36,319,490 (\$35,569,490 + \$150,000 + \$600,000), total estimated revenues related to 1994 submissions are \$57,663,550 (\$55,013,950 + \$300,600 + \$2,349,000), and total estimated revenues related to 1995 submissions are \$81,117,600 (\$64,240,800 + \$2,992,800 + \$13,884,000). These amounts exceed the appropriations of \$36,000,000 for 1993, \$56,284,000 for 1994, and \$79,423,000 for 1995. Surplus collections will be accumulated by the Agency until further collections of fees from each FY are unlikely. At that point, the Agency will refund surplus collections, or provide credits, in proportion to the total fees paid for that FY by each component. We are unlikely to reach that point for 1993 fees until early 1996, for 1994 fees until early 1997, and for 1995 until early 1998.

Through FY 1995, fees were waived in the amounts of \$1,028,000 for FY 1993, \$1,990,650 for FY 1994, and \$3,746,600 for FY 1995. All waivers are applied to the fiscal year in which the application was submitted. A reserve for additional waivers and reductions of \$176,000, \$403,400, and \$803,600 has been recorded by the Agency for FYs 1993, 1994, and 1995, respectively. This represents Accounts Receivable for which collections have been deferred, pending final resolution of waiver requests.

A summary of waiver actions taken for FYs 1993, 1994, and 1995 is included in Appendix B.

## OBLIGATION OF USER FEE REVENUES

User fee revenue can be expended only for increases in the costs of resources allocated for the process for the review of human drug applications, compared with 1992 adjusted obligations. Allowable and excludable costs for the process for the review of human drug applications are defined in Appendix C.

### STATEMENT OF USER FEE OBLIGATIONS

|                                     | <u>FY 1993</u>            | <u>FY 1994</u>             | <u>FY 1995</u>             |
|-------------------------------------|---------------------------|----------------------------|----------------------------|
| Personnel Compensation and Benefits | \$2,135,000               | \$16,157,000               | \$33,294,000               |
| Building Alterations                | 2,085,000                 |                            | 471,000                    |
| Contract Services                   | 667,000                   | 12,895,312                 | 18,222,000                 |
| Equipment and Supplies              | 3,864,000                 | 10,045,606                 | 18,715,000                 |
| Other                               | <u>41,000</u>             | <u>6,780</u>               | <u>237,015</u>             |
| <b>TOTAL OBLIGATIONS:</b>           | <b><u>\$8,949,000</u></b> | <b><u>\$39,951,020</u></b> | <b><u>\$74,064,015</u></b> |

Consistent with the intent of the Act, FDA continued to increase the extent of its activities involved with its process for review of human drug and biologic applications in FY 1995 to improve and expedite this process. Accordingly, during FY 1995, the Agency obligated \$74,064,015 of the user fees collected.

In FY 1995, FDA continued to hire additional personnel to expedite the drug application process. FDA dedicated 1,277 FTE (Full Time Equivalents or staff years) to the review of human drug applications in the baseline. A total-time reporting study was undertaken in 1993 to determine the percentage of time each division devotes to user fee related activities. This allowed calculation of FTE related costs. The percentages are updated quarterly through additional time studies. The development of these user fee related costs associated with the review of human drug applications is described in Appendix D. Throughout FY 1995, the Agency utilized about 453 more FTE for user fee included activities than were utilized in 1992.

FDA's total expenditures for payroll from user fee funds in FY 1995 were \$33,294,000. This amount includes costs for the additional staff hired, as well as payroll cost increases for the 1,277 FTE dedicated to the review of human drug applications. These cost increases include promotions, periodic step increases, pay raises, and retention bonuses.

The Agency continued its efforts to enhance information systems to further integrate and strengthen the electronic information infrastructure for the drug approval process and administrative support. Enhancements included tracking and retrieval systems, state-of-the-art computer software/hardware, and upgraded communications capabilities. The Agency obligated approximately \$25.7 million to support the PDUFA enhancement initiatives.

- o Information Systems Infrastructure. The Agency's continued improvement of its information systems infrastructure has had an impact on achieving the PDUFA performance goals discussed in the Third Annual Performance Report (page 17). Both CDER and CBER have invested in state-of-the-art high performance computers and LAN systems to support the drug application reviews and other program-related requirements. In addition, the Agency has made progress in developing a client/server environment to support a review process on electronic submission and enhance internal and external communications. Approximately \$17.9 million was obligated for these initiatives.
- o ADP Contract Support. In FY 1995, the Agency continued to contract for consultation, design, and development of automated initiatives which will enable the Agency to improve the application review process in CDER and CBER (\$7.8 million). Examples of projects included in this effort are:

- Standard Nomenclature. The Standard Nomenclature project is intended to provide the FDA and industry with a thesaurus of standard terms for drug applications. The activity was funded in the areas of safety, toxicology, clinical laboratories, and demographic data. (\$3 million).

- CBER Tracking System. In achieving Goal 6, which is discussed on page 15 of the Third Annual Performance Report, CBER expended \$0.9 million to continue enhancements to its performance tracking system. As mentioned, the system is designed to track and monitor PDUFA-defined performance.

Contracts for other support services were increased in FY 1995 to cover necessary support functions related to the prescription drug review process. These increased services included: document control room contracts; drug registration and listing contract; an inter-agency agreement to support the Agency's research programs; and facility service and supply contracts covering such services as security, and mail delivery. A total of \$6.5 million was obligated for these contracts and support services.

The Agency continued to support its research related to the process for the review of human drug applications. New scientific equipment and related supplies were purchased to enhance the Agency's diagnostic and research capabilities (\$2.5 million). Additional information about research is included in Appendix D.

Other administrative costs for PDUFA-related activities included: travel costs to industry meetings, symposia, and conferences; both foreign and domestic inspection travel; administrative and telecommunications support; travel and transportation of household goods for new drug reviewers; and office supplies and miscellaneous expenses (\$6 million).

#### **YEAR END BALANCE**

At the end of FY 1993, FDA had cash collections totaling \$19,582,996, unbilled receivables totaling \$3,555,506, and billed receivables of \$732,494 for a total of \$23,870,996. At the end of 1994, the total balance FDA carried forward to the next FY was \$34,146,420, consisting of cash collections of \$33,362,220, and receivables of \$784,200. At the end of FY 1995, the total balance FDA is carrying forward, \$31,860,205, consists of cash collections of \$30,251,705, and receivables of \$1,608,500. The net result of operations in FY 1995 decreased the balance carried forward by \$2,286,215. The Agency will be revising its Financial Operating Plan annually to reflect current expenditure levels and updated support and investment requirements.

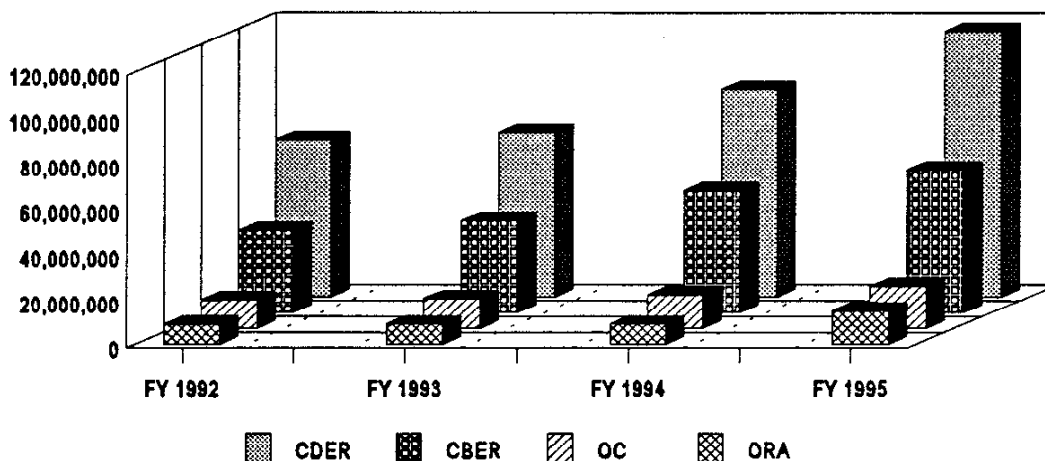
**TOTAL PROGRAM COSTS FOR THE PROCESS**  
**FOR THE REVIEW OF HUMAN DRUG APPLICATIONS**

The following table presents the costs for the review of human drug applications for FYs 1992, 1993, 1994, and 1995 by organizational component. This conveys the full cost of the process for the review of human drug applications, including costs paid from traditional appropriations, and, in 1993, 1994, and 1995, amounts from user fee revenues. The amounts are based upon obligations recorded as of the end of each FY. Over 81 percent of amounts obligated are expended within one year, and 96 percent within two years. Thus, obligations represent an accurate measure of costs.

**FOR THE FISCAL YEARS ENDED SEPTEMBER 30**

|  | <u>Adjusted 1992</u> | <u>1993</u>          | <u>1994</u>          | <u>1995</u>          |
|--|----------------------|----------------------|----------------------|----------------------|
| Costs for the Center for Drug Evaluation and Research (CDER)     | \$69,251,393         | \$72,618,726         | \$91,422,027         | \$117,065,219        |
| Costs for the Center for Biologic Evaluation and Research (CBER) | 36,179,338           | 40,511,011           | 53,805,952           | 63,103,088           |
| Field Inspection and Investigational Costs (ORA)                 | 8,877,245            | 9,054,944            | 9,038,316            | 15,053,823           |
| Agency General and Administrative Costs (OC)                     | <u>12,650,168</u>    | <u>13,279,896</u>    | <u>15,021,863</u>    | <u>18,672,203</u>    |
| <b>Total Cost for the Review of Human Drug Applications</b>      | <b>\$126,958,144</b> | <b>\$135,464,577</b> | <b>\$169,288,158</b> | <b>\$213,894,333</b> |

### Total Program Costs by Organizational Component



### MANAGEMENT CHALLENGES FOR FY 1996

The Prescription Drug User Fee Act has provided significant additional revenue to expedite the review of human drug applications. As demonstrated in the Third Annual Performance Report to Congress for FY 1995, these additional resources have been used to achieve the statutory performance goals established by the Act by reducing the average time between the submission of an application and the delivery of a first action. For FY 1996, FDA expects to continue to apply user fees to assure that the statutory performance goals for FY 1996 and 1997 are also attained. FDA will also continue aligning its incremental resources to changing workload requirements to ensure that a reasonable balance and real value to the regulated industry are maintained. The Agency is dedicated to ensuring that user fees paid by industry are effectively used for purposes supported by the Act.

Among the most pressing challenges facing the Agency is the need to continue to hire, equip, and train qualified reviewers and inspectors. Access to qualified, highly motivated reviewers and inspectors is essential to continued improvement in the human drug application review process. The percentage of user fees applied to this important effort as well as to the salaries and benefits of such employees should continue to grow.

Multi-year investments in information technologies and management systems that were begun in FYs 1994 and 1995 will continue. Both CDER and CBER have placed a high priority on and are making substantial investments in new technologies to improve the management of the application process and to support electronic submissions of applications. Investments such as these are necessary now in order to sustain a high level of performance in the future.

Without the availability of funds derived from user fees, it is unlikely that the substantial progress in improving and expediting the review of human drug applications could have been achieved. The challenge for FY 1996 will be to sustain and advance this achievement through the continued judicious use of these resources.

**CONDITIONS FOR ASSESSMENT AND USE OF FEES**

The Prescription Drug User Fee Act (The Act) enumerates three major conditions that must be met each year before fees can be collected and spent that year for the human drug review process. Each of these conditions is reviewed below, along with an explanation of how the condition was met in 1995.

The **first condition** comes from section 736(f)(1) of the Act. It states:

Fees may not be assessed under subsection (a) for a FY beginning after FY 1993 unless appropriations for salaries and expenses of the FDA for such FY (excluding the amount of fees appropriated for such FY) are equal to or greater than the amount of appropriations for the salaries and expenses of the FDA for the FY 1992 multiplied by the adjustment factor applicable to the FY involved.

The Act requires that the 1992 Salaries and Expenses appropriation for FDA will be adjusted each year by an "adjustment factor", which is defined in section 735(8) of the act. It states:

The term 'adjustment factor' applicable to a FY is the lower of-

- (A) the Consumer Price Index for all urban consumers (all items; United States city average) for August of the preceding FY divided by such Index for August 1992, or
- (B) the total of discretionary budget authority provided for programs in the domestic category for the immediately preceding FY (as reported in the Office of Management and Budget sequestration preview report, if available, required under section 254(d) of the Balanced Budget and Emergency Deficit Control Act of 1985) divided by such budget authority for FY 1992 (as reported in the Office of Management and Budget final sequestration report submitted after the end of the 102d Congress, 2d Session).

The FDA used the first calculated factor, 5.748%. Applying this to the FY 1992 appropriation of \$725,962,000 the adjusted FY 1992 appropriation is \$767,690,296. FDA's FY 1995 Salaries and Expenses Appropriation, excluding user fees, was \$817,681,000. Therefore, the first condition was met.

The **second condition** comes from Section 736 (g) (2) (A). It states that fees shall be collected in each year in an amount specified in appropriation Acts for that FY. Without a specific appropriation, no fees may be collected.

The basic appropriation act specifying amounts collectable from fees during FY 1995 (Public Law 103-330) was signed by the President September 30, 1994. This appropriation provided that \$79,423,000 in funding was to come from fees collected under the Act, and specified that the fees collected could remain available until expended. Thus, the second condition was met.

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

“shall only be collected and available to defray increases in the costs of the resources allocated for the process for the review of human drug applications (including increases in such costs for an additional number of full-time equivalent positions in the Department of Health and Human Services to be engaged in such process) over such costs for FY 1992 multiplied by the adjustment factor.”

The following table summarizes the obligations for the process for the review of human drug applications and compares the level of spending from base FDA resources.

**OBLIGATIONS FOR THE PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS**

|                     | <u>Adjusted FY 1992</u> | <u>FY 1995</u>       |
|---------------------|-------------------------|----------------------|
| Base Appropriations | \$126,958,144           | \$139,830,318        |
| User Fee Funds      | <u>\$0</u>              | <u>\$74,064,015</u>  |
| Total Obligations   | <u>\$126,958,144</u>    | <u>\$213,894,333</u> |



**WAIVERS AND EXEMPTIONS**

The Act directs FDA to waive or reduce fees in five different circumstances:

- when a waiver is necessary to protect the public health;
- when a fee is a significant barrier to innovation;
- when the fees paid exceed FDA's costs of reviewing a person's human drug application;
- when imposition of the fee creates an inequity between certain 505(b) (1) and 505(b) (2) human drug applications and;
- when a sponsor withdraws a pending human drug application after FDA has filed it, but before FDA has performed substantial work on the marketing application.

All fees may be waived or reduced under these waiver provisions. Many of the waiver requests FDA receives pertain to orphan products, products indicated for diseases or conditions affecting fewer than 200,000 patients in the United States. FDA reviews waiver requests on a case by case basis, taking into account, among other things, the patient population for which a drug product is indicated.

The Act also directs FDA to permit qualified small businesses to defer payment of application fees for one year after submission of a human drug application, and to reduce the application fee by 50 percent. To qualify for the small business exemption, a business must have fewer than 500 employees, and have no prescription drug products introduced into interstate commerce.

The following table summarizes the waiver actions taken by FDA for FYs 1993, 1994, and 1995:

## APPROVED WAIVERS

|   | <u>FY 1993</u>            | <u>FY 1994</u>            | <u>FY 1995</u>            |
|---|---------------------------|---------------------------|---------------------------|
| <b>APPLICATIONS:</b>                        |                           |                           |                           |
| Waivers Approved                            | 8                         | 8                         | 12                        |
| Value of Waivers Approved                   | <u>\$650,000</u>          | <u>\$883,250</u>          | <u>\$2,392,000</u>        |
| <b>PRODUCTS:</b>                            |                           |                           |                           |
| Waivers Approved                            | 19                        | 32                        | 29                        |
| Value of Waivers Approved                   | <u>\$138,000</u>          | <u>\$357,000</u>          | <u>\$463,600</u>          |
| <b>ESTABLISHMENTS:</b>                      |                           |                           |                           |
| Waivers Approved                            | 4                         | 8                         | 7                         |
| Value of Waivers Approved                   | <u>\$240,000</u>          | <u>\$750,400</u>          | <u>\$891,000</u>          |
| <b>TOTAL VALUE OF<br/>WAIVERS APPROVED:</b> | <b><u>\$1,028,000</u></b> | <b><u>\$1,990,650</u></b> | <b><u>\$3,746,600</u></b> |

## PENDING WAIVERS

|   | <u>FY 1993</u>          | <u>FY 1994</u>          | <u>FY 1995</u>          |
|---|-------------------------|-------------------------|-------------------------|
| <b>APPLICATIONS:</b>                            |                         |                         |                         |
| Waivers Pending                                 | 1                       | 0                       | 9                       |
| Allowance for Pending Waivers                   | <u>\$50,000</u>         | <u>\$0</u>              | <u>\$0<sup>1</sup></u>  |
| <b>PRODUCTS:</b>                                |                         |                         |                         |
| Waivers Pending                                 | 1                       | 3                       | 13                      |
| Allowance for Pending Waivers                   | <u>\$6,000</u>          | <u>\$28,200</u>         | <u>\$158,600</u>        |
| <b>ESTABLISHMENTS:</b>                          |                         |                         |                         |
| Waivers Pending                                 | 2                       | 4                       | 5                       |
| <hr/>   |                         |                         |                         |
| <b>TOTAL ALLOWANCE FOR<br/>PENDING WAIVERS:</b> | <b><u>\$176,000</u></b> | <b><u>\$403,400</u></b> | <b><u>\$803,600</u></b> |

<sup>1</sup> No allowance was established for FY 1995 application waivers pending because, for the firms who submitted waiver requests, there were no outstanding accounts receivable.

**ALLOWABLE AND EXCLUDED COSTS FOR THE PROCESS FOR THE  
REVIEW OF HUMAN DRUG APPLICATIONS**

The Prescription Drug User Fee Act of 1992 and the related House of Representatives Report 102-895 ("House Report") define, for the first time, the process for the review of human drug applications and the costs which may be included in that process. Using these definitions (and further refinements as necessary) and the methodologies described in this report, the Agency identified those activities which were applicable to the process for the review of human drug applications. The costs of resources allocated to the process for the review of human drug applications are based on FY 1992 and 1995 obligations, which are consistent with the FY 1992 and 1995 appropriations referenced in the Act. Over 96 percent of amounts obligated are expended within two years. Thus, obligations represent an accurate measure of costs.

**User Fee Related Costs**

Section 735(6) of the Act defines in general terms the activities necessary for the review of human drug applications (the "human drug review process"). In summary, costs related to the following process activities have been attributed to the process for the review of human drug applications.

- All investigational new drug (IND) review activities (including amendments), after an IND exemption has become effective pursuant to section 505(I) of the Federal Food, Drug, and Cosmetic Act .
- All new drug application (NDA) and product license application (PLA) review activities (including supplements and amendments).
- All review activities for establishment license applications (ELAs) and amendments.
- Regulation and policy development activities related to the review of human drug applications.
- Development of product standards for products subject to review and evaluation.
- Meetings between the Agency and the sponsor of a covered application or supplement.
- Review of labeling prior to approval of a covered application or supplement and the review of the initial pre-launch advertising.
- Review of post-marketing studies that have been agreed to by sponsors as a condition for approval.
- Inspections of facilities undertaken as part of the review of pending applications or supplements.
- Lot release activities for covered biological products.
- Assay development and validation to ensure batch-to-batch consistency and reliability for covered biological products.
- Monitoring of clinical and other research conducted in connection with the review of human drug applications.
- User Fee Act implementation activities.
- Research related to the human drug review process .

All user fee related costs represented by the above activities are collectively referred to in this report as costs for the process for the review of human drug applications.

Section 735(7) of the Act defines the "costs of resources allocated for the process for the review of human drug applications" as the expenses incurred in connection with this process for :

- (A) officers and employees of the FDA, employees under contract with the FDA who work in facilities owned or leased for the FDA, advisory committees, and costs related to such officers, employees, and committees including, travel, education, recruitment, and other personnel related activities;
- (B) management of information, and the acquisition, maintenance, and repair of computer resources;
- (C) *leasing, maintenance, renovation, and repair of facilities and acquisition, maintenance, and repair of fixtures, furniture, scientific equipment, and other necessary materials and supplies; and*
- (D) collecting user fees under section 736 of the Act and accounting for resources allocated for the review of human drug applications and supplements.

#### **User Fee Excluded Costs**

The User Fee Act excludes costs related to the following.

#### **Excluded Products**

- Generic drugs
- Over-the-counter drugs not associated with an NDA or NDA supplement
- Large volume parenterals approved before 9/1/92
- Allergenic extract products
- Whole blood or a blood component for transfusion
- In vitro diagnostic biologic products
- Certain drugs derived from bovine blood

#### **Excluded Process Activities**

- Pre-IND effective activities
- Enforcement policy development
- Post-approval compliance activities
- Advertising review activities once marketing of the product has begun
- Inspections unrelated to the review of covered applications
- Research unrelated to the human drug review process

Since these inclusions and exclusions require an accounting of a subset of FDA activities, it was necessary to develop and implement a methodology that would allow the Agency retrospectively to capture the 1992 costs for the newly defined "process for the review of human drug applications," and apply that same methodology for future year calculations. Arthur Andersen & Company independently reviewed FDA procedures in 1995, and found the methodologies to be reasonable.

**DEVELOPMENT OF COSTS FOR THE  
PROCESS FOR THE REVIEW OF HUMAN DRUG APPLICATIONS**

**GENERAL METHODOLOGY**

The costs associated with the process for the review of human drug applications are based upon obligations recorded within the following FDA organizations: the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) (together - "center costs"), the Office of Regulatory Affairs (ORA), and the Office of the Commissioner (OC). These organizations correspond to the cost categories presented on the Statement of Costs for the Process for the Review of Human Drug Applications as follows:

| <u>Cost Category</u>  | <u>FDA Organization</u> |
|---|-------------------------|
| Costs for the Review of New Drug Applications and Supplements     | CDER                    |
| Costs for the Review of New Biologic Applications and Supplements | CBER                    |
| Field Inspection and Investigation Costs                          | ORA                     |
| Agency General and Administrative Costs                           | OC                      |

The costs were accumulated using a variety of methods including time reporting, management surveys, and detailed interviews. Using the definitions of costs and activities included in the "process for the review of human drug applications" in the Act, a portion of the costs within the four organizations listed above was identified as part of the human drug review process.

In addition, in 1994, OC established the Strategic Systems Staff as a part of the Office of Management and Systems. This staff was tasked with the development of computer systems designed to provide management information necessary to the proper implementation of the Act.

**Center Costs**

Costs are accumulated in CDER and CBER in cost centers corresponding to the organizational divisions within the centers. Most FDA divisions involved in the human drug review process perform a mixture of user fee included activities and user fee excluded activities. These divisions fall into three categories: 1) review and laboratory divisions; 2) indirect review and support divisions; and 3) user fee excluded divisions. Costs are accumulated in division cost centers, as well as cost centers which collect center-wide expenses applicable to some or all of the divisions

in a center. The allocation of costs for the three categories of divisions and centerwide expenses are discussed below.

**Review and Laboratory Divisions:**

The review and laboratory divisions, as organized during FY 1995, have the primary responsibility for the review of human drug applications and supplements. Below is a list of the direct review and laboratory divisions in CDER and CBER.

| <b>REVIEW AND LABORATORY DIVISIONS</b>    |   |
|---|---|
| <b>CDER</b>                               | <b>CBER</b>                               |
| Office of the Center Director             | Office of the Center Director             |
| Office of Drug Evaluation 1               | Office of Vaccines                        |
| Office of Drug Evaluation 2               | Office of Therapeutics                    |
| Cardio Renal                              | Office of Blood                           |
| Neuropharmacology                         | Allergenic Products and Parasitology      |
| Oncology and Pulmonary                    | Bacterial Products                        |
| Medical Imaging Surgical-Dental           | Viral Products                            |
| Gastrointestinal and Coagulation          | Vaccines and Related Product Applications |
| Metabolism and Endocrine                  | Cytokine Biology                          |
| Anti-Infective                            | Cellular and Gene Therapies               |
| Anti-Viral                                | Hematologic Products                      |
| Biopharmaceutics                          | Clinical Trial Design and Analysis        |
| Pilot Drug Evaluation                     | Application Review and Policy             |
| Biometrics                                | Transfusion Transmitted Diseases          |
| Office of Over the Counter Products       | Hematology                                |
| Division of Drug Advertising              | Blood Applications                        |
| Division of Epidemiology and Surveillance | Establishment Licensing                   |
| Division of Topical Drug Products         | Biostatistics and Epidemiology            |
|   | Biological Product and Quality Control    |
|   | Monoclonal Antibodies                     |
|   | Veterinary Services                       |

User fee related activities in the direct review and laboratory divisions were measured using two methodologies. During 1993, a 16-week total time reporting study was conducted in CDER and CBER among all direct review personnel to measure the level of user fee related costs for each of these divisions.

These time reporting data were used to measure user fee related costs in CDER for FY 1994 and FY 1992. In CBER, a workload measurement procedure, in place since 1991 for planning purposes, was conducted among CBER staff to assess level of effort expended by each division on certain pre-defined activities. A total of 43 possible

functional activities by 9 product classes were reported. These data were used to determine the user fee related costs for all divisions in CBER in FYs 1992, 1994, and 1995.

#### Indirect Review and Support Divisions

Indirect review and support divisions assist the primary review divisions and provide the infrastructure for the review process. In CDER, these divisions include *bioresearch monitoring, information systems, management and budget, and the medical library*. In CBER these divisions include the Immediate Office of the Center Director, Office of Management, and Office of Compliance.

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

In CBER, the workload measurement procedures were used to measure the level of user fee related activities in the compliance divisions. The Office of the Director and the Office of Management are considered support organizations to CBER, therefore their actual time is added as overhead to each activity.

#### User Fee Excluded Divisions

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

#### Center-wide Expenses

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



## **TIME REPORTING STUDY**

A total time reporting study was conducted from July 18, 1993, to November 6, 1993, as part of a contract with Arthur Andersen & Company, to measure the level of user fee related activities for the direct review and laboratory divisions in CDER and CBER. Over 1,000 staff participated in the 16-week study. The time sheets were designed to capture information on activities based on the definitions for the process for the review of human drug applications in the Act.

Using the results of the time reporting study, a user fee related percentage was calculated for each participating division and applied to the total FY 1992. The results of the 16-week time reporting exercise are representative of the activities during FYs 1992, 1993, and 1994 in CDER. In CBER, the original workload measurement procedure was used to measure 1992 and 1994 user fee costs. The results of the Arthur Andersen & Company 16 week total time reporting study were used to measure CBER's 1993 user fee costs.

In May 1995, CDER conducted an internal time reporting study of all CDER units previously surveyed by Arthur Andersen in 1993. This internal study enabled CDER to update user fee percentages on a one-time basis. On November 19, 1995, CDER implemented on-line, quarterly time reporting. These quarterly updates will facilitate timely reporting of user fee percentages by the various components of the Center.

In FY 1995, CBER began collecting, quarterly, based on the 1993 Arthur Andersen survey, "all hands" actual hours worked reported over a 2-3 consecutive week period. A total of 43 possible functional activities by 9 product classes were reported. Research activity was reported by specific research project number. These quarterly surveys were used to calculate the Center's PDUFA activity for each quarter and the percentage applied to each cost center. By mid-1995, CBER had begun a pilot computer-based reporting system (mirroring the paper submissions), that was accessed through the network (paperless.) By the end of the fiscal year, CBER designed, with the assistance of Arthur Andersen, an on-line reporting system called the Resources Reporting System, that would be easier for employees to report and would provide more data to management.

Additionally, the Resource Reporting System links direct review time to other Center data systems for application review and to the research project database. CBER has designed downloading capabilities to generate PDUFA percentage reports and other management information for both the Agency and the Center.

## **RESEARCH COVERED BY THE PRESCRIPTION DRUG USER FEE ACT**

The FDA performs research to determine the risks and benefits of pharmaceutical agents and to set appropriate standards and methods for analysis. These activities include research on specific products or product classes that are approved or under review. Research is carried out in biomedical areas to develop expertise necessary to address new technologies, issues and emerging areas, develop and validate testing methodologies, and to establish drug and biologic standards.

All of these activities are fundamental to the evaluation of human drugs and biological products. Research activities that directly support the process for the review of drug and biologic applications are described below.

Laboratory activities specified in the legislative history of PDUFA that are associated with the drug review process include activities necessary for the release of lots of biologics under section 351 of the PHS Act, and assay development and validation to ensure batch-to-batch consistency and reliability.

Further, the FDA Fee Management Committee defined research activities associated with the review of new drugs and biologics such as research to facilitate review of clinical and product testing, support policy development, validate assays, and develop standards. These user fee related activities are associated with approved products or product classes, those currently under review as IND's, PLA's, NDA's, or supplements.

Laboratory activities that are associated with generic drugs, OTC monographs, allergenic

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are excluded from coverage as described in the Act.

The time reporting study undertaken in 1993 determined the extent of resources expended on research covered by PDUFA. Time was reported to individual research projects and each project was reviewed to determine whether it met the criteria for coverage by the user fee program. These related costs were aggregated and included in the appropriated baseline for PDUFA. Periodic time surveys are undertaken to update these costs. In FY 1995, CBER implemented a program, as a part of their time reporting system, to capture research time by individual research project.

### Types of Research

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

#### **Review of the Manufacturing Process**

The evaluation of new biological and drug products requires a careful review of the manufacturing process. The process of manufacture can potentially result in subtle changes in the product characteristics which could affect safety and efficacy of the product. This review is especially critical in the evaluation of new products manufactured using new technologies.

#### **Development and Validation of Test Methodologies**

Standards for testing must be set for each drug or biologic product in order to ensure its identity, purity, and potency prior to approval. Frequently, test methods are developed

and validated in FDA laboratories. These tests are used for lot release and for characterizing qualification lots of products submitted for approval.

### Safety and Toxicity

New drugs and biological products must be evaluated for safety and toxicity. Frequently, a product will represent a new class whose toxicity profile is not well established. In these cases, it may be necessary for the Agency to conduct studies to gain information in order to establish policy and safety standards for similar products in the new product class.

### Pharmacology

The pharmacology of drugs and biological products must be understood in order to evaluate potential toxicities and measures of potency. In some cases a detailed understanding of the mechanisms of action, metabolism, distribution, and excretion is critical to establish tests for potency and to better understand toxicity. It may also be necessary for pharmacodynamic endpoints to establish appropriate product dosing and to develop in-vivo and in-vitro standards for evaluating manufacturing changes.

### Clinical

The study of drugs and biological products in human subjects is an important component of FDA research. Many important questions related to the optimal use of a given drug in human subjects or patients may not be part of the standard drug development process. However, such data would facilitate more optimal use of the product. Further, some of these research questions impact on regulatory review policy for the product class being studied. Examples of such research include the study of drugs in special populations (i.e. women, the elderly, patients with renal or hepatic impairment), evaluation of drug interactions and the development of pharmacokinetic/pharmacodynamic correlations, or safety of combination vaccines.

## FIELD INSPECTION AND INVESTIGATION COSTS

All field inspection and investigation costs are generated by FDA's Office of Regulatory Affairs (ORA). ORA costs are incurred in both the ORA administrative office and the district offices (the "field"). The primary human drug review activities performed in the field are inspections of manufacturing facilities, investigations of clinical studies, and analytical testing of samples. The Agency accumulates ORA fee related cost data through the use of the Program Oriented Data System (PODs). PODs is a time tracking system which captures both CDER and CBER pre-approval inspection, investigation, and analytical hours.

The ORA user fee related costs are calculated from the amount of FTEs (full time equivalents, or staff years of effort) used in the human drug review process. Based upon a description of the work performed in PODs (which is tracked by Program Assignment Code), the Agency accumulates total direct hours incurred on pre-approval activities related to the human drug review process. Total direct hours is used to calculate the total number of FTEs required by ORA to perform these activities. In addition to the direct FTEs, an allocation of support FTEs is also included to represent the work done by the ORA administrative/management personnel. The Agency then applies the total number of user fee related FTEs to the average salary cost in ORA to arrive at ORA user fee related salary costs. The final step is to allocate ORA obligations for operations and rent to the human drug review process based upon the level of user fee related FTEs to total ORA FTEs. The following table summarizes the calculation for the FYs ended September 30, 1992, 1993, 1994, and 1995.

### **PROCESS RELATED COSTS FOR THE OFFICE OF REGULATORY AFFAIRS**

|   | <u>Adjusted</u>           |                           |                           |                            |
|---|---------------------------|---------------------------|---------------------------|----------------------------|
|   | <u>1992</u>               | <u>1993</u>               | <u>1994</u>               | <u>1995</u>                |
| FTEs Related to Pre-Approval Activities | 73.55                     | 78.12                     | 73.48                     | 107.01                     |
| ORA Administrative/Management FTEs      | <u>52.96</u>              | <u>56.24</u>              | <u>52.92</u>              | <u>77.05</u>               |
| Total Process Related FTEs              | 126.51                    | 134.36                    | 126.40                    | 184.06                     |
| Average Salary and Benefits in ORA      | <u>\$46,023</u>           | <u>\$47,713</u>           | <u>\$51,083</u>           | <u>\$54,654</u>            |
| Process Related Salary and Benefits     | 5,822,403                 | 6,410,696                 | 6,456,849                 | 10,059,623                 |
| Process Related Operations and Rent     | 2,572,314                 | <u>2,644,248</u>          | <u>2,281,468</u>          | <u>4,994,200</u>           |
| FY 1992 Adjustment <sup>2</sup>         | <u>482,528</u>            |                           |                           |                            |
| <b>ORA PROCESS RELATED COSTS</b>        | <b><u>\$8,877,245</u></b> | <b><u>\$9,054,944</u></b> | <b><u>\$9,038,316</u></b> | <b><u>\$15,053,823</u></b> |

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<sup>2</sup> The FY 1992 Adjustment amount is for comparison to FY 1995 costs only.

## **AGENCY GENERAL AND ADMINISTRATIVE COSTS**

The agency general and administrative costs are generated in the FDA's Office of the Commissioner (OC). OC is comprised of the following offices:

- Immediate Office of the Commissioner
- Office of Policy
- Office of External Affairs
- Office of Management and Systems

The OC costs applicable to the process for the review of human drugs was calculated per a method developed by the Division of Cost Determination Management, Office of Finance, Office of the Secretary, Department of Health and Human Services. The method calls for an allocation based on the total salary obligations of the Agency's operations. The calculated allocation rate is applied to the combined salaries applicable to the process for the review of human drugs in CDER and CBER, and ORA to arrive at the OC allocation.

Accordingly, \$12,650,168 and \$18,672,203 in OC obligations were allocated to the human drug review process in FYs 1992 and 1995, as adjusted, respectively.