supplements submitted on or after October 1, 1995, FDA will refund applicants for the difference between fees paid and fees due under the new fee schedules. For applications and supplements submitted after December 31, 1995, the new fee schedule should be used. Invoices for establishment and product fees for FY 1996 will be issued in December 1995, using the new fee schedules.

I. Revenue Increase and Fee Adjustment Process

The PDUFA provides that total fee revenues for each FY, as set out in the original fee schedule (see 21 U.S.C. 379h(b)(1)), shall be increased by notice in the Federal Register. The increase must reflect the greater of : (1) The total percentage increase that occurred during the FY in the Consumer Price Index (the CPI) (all items; U.S. city average), or (2) the total percentage pay increase for that FY for Federal employees, as adjusted for any localitybased payment applicable to employees stationed in the District of Columbia (see 21 U.S.C. 379h(c)(1)). The PDUFA also provides that within 60 days after the end of each FY, FDA shall adjust the user fee rates in each of the three categories of fees (application, establishment, and product) to achieve the revised total fee revenues. The new individual user fees must be adjusted in a manner that maintains the proportions established in the original fee schedules, so that approximately one-third of the revenues will come each from applications, establishments, and product fees (21 U.S.C. 379h(c)(2)).

III. Total Fee Revenue Adjustment

For FY 1995, the total percentage increase in the CPI was 2.54 percent, whereas the increase in applicable Federal salaries for FY 1996 is 2.54 percent. Thus, for computing the total fee revenues for FY 1996, the percentage is 2.54. The new adjusted total fee revenue is computed by applying the increase as a percentage (102.54 percent) to the FY 1996 target fee revenue amount from the PDUFA schedule (\$78 million). The FY 1996 total adjusted fee revenue amount then totals \$79,981,200.

IV. Fee Calculations for Application, Establishment, and Product Fees

The PDUFA provides that in making adjustments to the user fee rates, the one-third proportionality must be maintained among application, product, and establishment fees. Thus, the amount of revenues to be obtained from each category are \$26,660,400 (\$79,981,200 divided by 3).

A. Application Fees

Application fees are assessed on each "human drug application," as defined in the PDUFA (see 21 U.S.C. 379g(1)). Application fees are levied for: (1) Review of certain new drug applications submitted after September 1, 1992, under section 505(b)(1) of the act (21 U.S.C. 355(b)(1)); (2) for review of an application for certain molecular entities or indications for use submitted after September 30, 1992, under section 505(b)(2) of the act; (3) review of applications for initial certifications or approvals of antibiotic drugs submitted after September 1, 1992, under section 507 of the act (21 U.S.C. 357); and (4) for review of applications for licensure of certain biological products under the Public Health Service Act (42 U.S.C. 262).

Fees are assessed at different rates for qualifying applications depending on whether the applications require clinical data on safety and 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 with clinical data.

In most cases, a first payment of 50 percent of an application or supplement fee is due at the time the application or supplement is submitted (21 U.S.C. 379h(a)(1)(B)(i)). The final payment is due 30 days from the date FDA issues an invoice after issuance of an action letter for the application (see 21 U.S.C. 379g(6)(B)), or at the time an application is withdrawn, unless FDA waives this portion of the fee (21 U.S.C. 379h(a)(1)(A)(ii)). If FDA refuses to file an application or supplement, one-half of the first payment is refunded to the applicant (21 U.S.C. 379h(a)(1)(D)).

In setting the specific rate for each type of fee, FDA is required to estimate the numbers of applications, supplements, establishments, and products that it expects will qualify for fees in FY 1996. FDA makes this estimate based on the number of products, establishments, or applications subject to fees in FY 1995.

For FY 1995, FDA received and assessed fees for 87 filed applications that require clinical data, 36 applications that did not require clinical data, and 62 supplements that require clinical data. Because applications that do not require clinical data and supplements that require clinical data are assessed only one-half the full fee (that is, one-half the fee due on an application that requires clinical data), 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 subject to full application fees.

In addition, as of September 30, 1995, FDA refused to file, or there were withdrawn before filing, two applications that required clinical data, and four applications that did not require clinical data. After refunds, each of the former applications paid onefourth the full application fee and are counted as one-fourth of an application. Similarly, after refunds, each of the latter applications paid one-eighth of the full application fee rate and are counted as one-eighth of an application.

Using this methodology, the approximate equivalent number of applications that required clinical data and were assessed fees in FY 1995 was 137, before any further decisions were made on requests for waivers or reductions. Additional waivers or reductions of FY 1995 fees are expected to account for approximately 6 equivalents of applications that require clinical data. Therefore, FDA estimates that approximately 131 equivalent applications that require clinical data will qualify for fees in FY 1996, after allowing for possible waivers or reductions. Thus, the FY 1996 application fee rate is determined by dividing the adjusted total fee revenue to be derived from applications (\$26,660,400) by the equivalent number of applications projected to qualify for fees in FY 1996 (131), for a fee of \$204,000 per application that requires clinical data (rounded to the nearest \$1,000). A fee of one-half this amount or \$102,000 applies to applications that do not require clinical data and to supplements that require clinical data. The following calculations summarize the determination of FY 1996 application fee rates:

• 87 applications that require clinical data, + (36+2) applications that do not require clinical data, + (62+2) supplements that require clinical data, + (2+4) applications that require clinical data and which FDA refuses to file or the sponsor withdraws before filing, + (4+8) other applications that FDA refuses to file or the sponsor withdraws before filing minus 6 waivers or reductions = 131 (the estimated number of "full fee" applications for FY 1996 based on FY 1995 experience).

• \$26,660,400 (FY 1996 estimated revenue to be derived from applications)