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Comments about the draft guidance documents will be considered by the FDA and the VICH Safety Working Group.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This draft guidance document, developed under the VICH process, has been revised to conform to FDA's good guidance practices regulation (65 FR 56468, September 19, 2000).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 Similarly, words such as ''require'' or ''requirement'' have been replaced by ''recommendation'' or ''recommended'' as appropriate to the context.

The draft guidance document represents the agency's current thinking on genotoxicity safety studies for veterinary drug residues in human food.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This draft guidance document is being distributed for comment purposes only and is not intended for implementation at this time. Interested persons may submit to the Dockets Management Branch (address above) written comments regarding this draft guidance document.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

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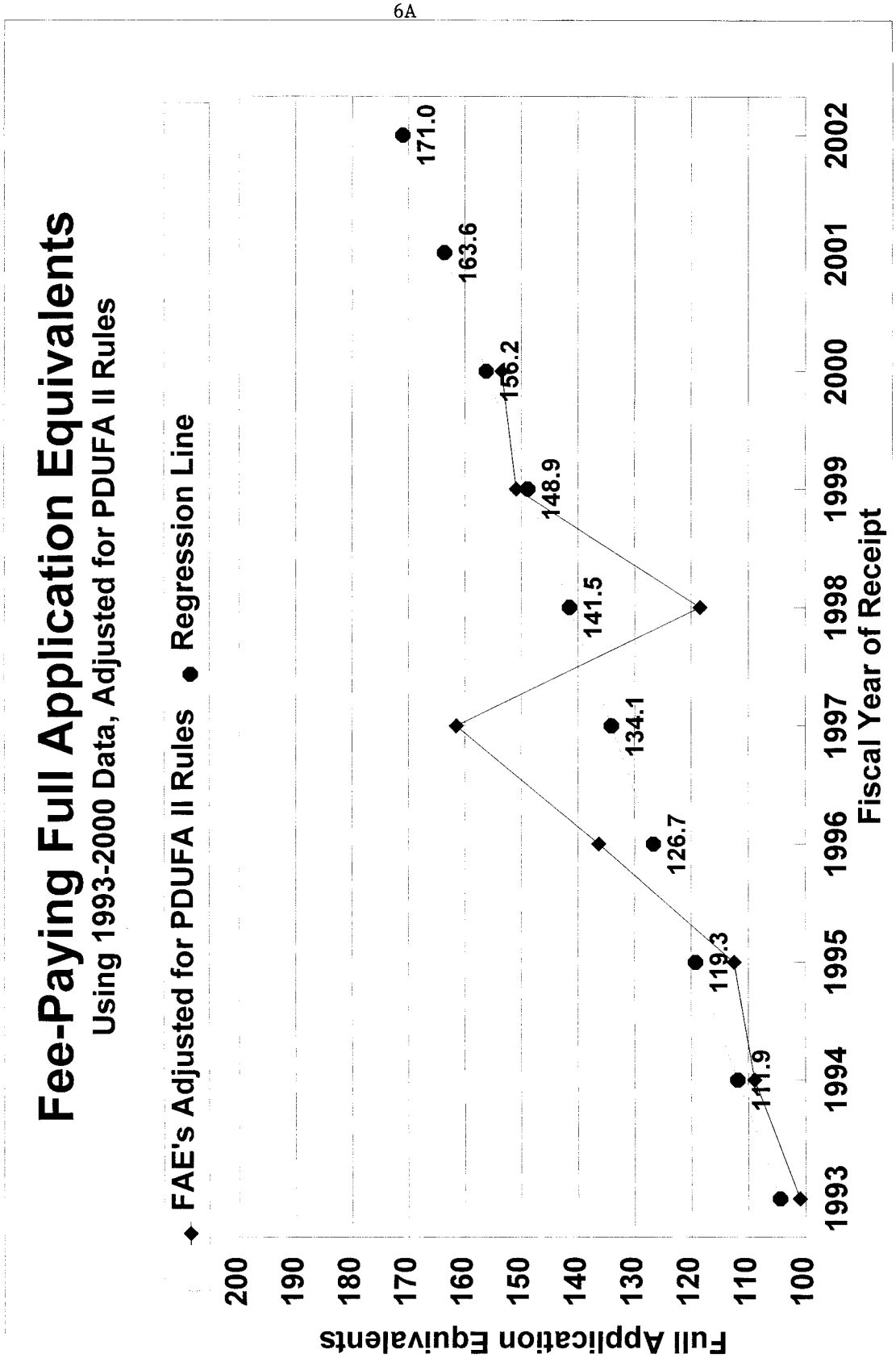

Regression Analysis/Projection based on Actual Data through FY 2000

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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]

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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.