

### Certification Regarding Drug-Free Workplace Requirements

#### Alternate I. (Grantees Other Than Individuals)

The grantee certifies that it will or will continue to provide a drug-free workplace by:

(a) Publishing a statement notifying employees that the unlawful manufacture, distribution, dispensing, possession, or use of a controlled substance is prohibited in the grantee's workplace and specifying the actions that will be taken against employees for violation of such prohibition;

(b) Establishing an ongoing drug-free awareness program to inform employees about—

(1) The dangers of drug abuse in the workplace;

(2) The grantee's policy of maintaining a drug-free workplace;

(3) Any available drug counseling, rehabilitation, and employee assistance programs; and

(4) The penalties that may be imposed upon employees for drug abuse violations occurring in the workplace;

(c) Making it a requirement that each employee to be engaged in the performance of the grant be given a copy of the statement required by paragraph (a);

(d) Notifying the employee in the statement required by paragraph (a) that, as a condition of employment under the grant, the employee will—

(1) Abide by the terms of the statement; and

(2) Notify the employer in writing of his or her conviction for a violation of a criminal drug statute occurring in the workplace no later than five calendar days after such conviction;

(e) Notifying the agency in writing, within 10 calendar days after receiving notice under paragraph (d)(2) from an employee or otherwise receiving actual notice of such conviction. Employers of convicted employees must provide notice, including position title, to every grant officer or other designee on whose grant activity the convicted employee was working, unless the Federal agency has designated a central point for the receipt of such notices. Notice shall include the identification number(s) of each affected grant;

(f) Taking one of the following actions, within 30 calendar days of receiving notice under paragraph (d)(2), with respect to any employee who is so convicted —

(1) Taking appropriate personnel action against such an employee, up to and including termination, consistent with the requirements of the Rehabilitation Act of 1973, as amended; or

(2) Requiring such employee to participate satisfactorily in a drug abuse assistance or rehabilitation program approved for such purposes by a Federal, State, or local health, law enforcement, or other appropriate agency;

(g) Making a good faith effort to continue to maintain a drug-free workplace through implementation of paragraphs (a), (b), (c), (d), (e) and (f).

(B) The grantee may insert in the space provided below the site(s) for the

performance of work done in connection with the specific grant:

Place of Performance (Street address, city, county, state, zip code) .

Check if there are workplaces on file that are not identified here.

#### Alternate II. (Grantees Who Are Individuals)

(a) The grantee certifies that, as a condition of the grant, he or she will not engage in the unlawful manufacture, distribution, dispensing, possession, or use of a controlled substance in conducting any activity with the grant;

(b) If convicted of a criminal drug offense resulting from a violation occurring during the conduct of any grant activity, he or she will report the conviction, in writing, within 10 calendar days of the conviction, to every grant officer or other designee, unless the Federal agency designates a central point for the receipt of such notices. When notice is made to such a central point, it shall include the identification number(s) of each affected grant.

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. 2007N-0005]

#### Prescription Drug User Fee Act; Public Meeting

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of public meeting.

**SUMMARY:** The Food and Drug Administration (FDA, we) is publishing proposed recommendations for the reauthorization of the Prescription Drug User Fee program for the process of human drug application review for fiscal years (FY) 2008 to 2012. These proposed recommendations were developed after discussions with regulated industry and consultation with appropriate scientific and academic experts, healthcare professionals, and representatives of patient and consumer advocacy groups. Section 505 of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, enacted June 12, 2002, directs FDA to publish these proposed recommendations in the **Federal Register**; hold a meeting at which the public may present its views on such recommendations; and provide for a period of 30 days for the public to provide written comments on such recommendations.

**DATES:** The public meeting will be held on February 16, 2007, from 9 a.m. to 5

p.m. Submit written comments by February 23, 2007. Registration to attend the meeting must be received by February 2, 2007.

**ADDRESSES:** The meeting will be held at the Grand Hyatt Washington at Washington Center, 1000 H St. NW., Washington, DC 20001. Located at the Metro Center metro stop. Follow 11th St. exit to the lobby of the Grand Hyatt. For additional directions, see the hotel Web site at: <http://grandwashington.hyatt.com/hyatt/hotels/>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

#### FOR FURTHER INFORMATION CONTACT:

For information regarding this document, contact: Ann Sullivan, Office of Policy and Planning (HFP-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-5887, FAX: 301-827-5225, e-mail: [Ann.Sullivan@fda.hhs.gov](mailto:Ann.Sullivan@fda.hhs.gov).

For information regarding registration, contact: Bernadette Kawaley, Office of Communication, Training and Manufacturers Assistance (HFM-49), Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, suite 200N, Rockville, MD 20852, 301-827-2000, FAX: 301-827-3079.

#### SUPPLEMENTARY INFORMATION:

##### I. Introduction

The Prescription Drug User Fee Act (PDUFA I), first enacted in 1992 (Public Law 102-571, October 29, 1992), authorized FDA to collect user fees from regulated industry that were to be dedicated to expediting the review of human drug applications in accordance with certain performance goals identified in letters from the Secretary of Health and Human Services to the Chairman of the Energy and Commerce Committee of the House of Representatives and the Chairman of the Labor and Human Resources Committee of the Senate (138 Cong. Rec. H9099-H9100 (daily ed. September 22, 1992)). In 1997, as PDUFA I expired, Congress passed the Food and Drug Administration Modernization Act (FDAMA, Public Law 105-115). FDAMA included, among other things, an extension of PDUFA (PDUFA II) for an additional 5 years. In 2002, Congress extended PDUFA again for 5 years (PDUFA III) through the Public Health

Security and Bioterrorism Preparedness and Response Act (Public Law 107–188).

Before PDUFA, FDA's review process was more unpredictable, and slower. At the same time, regulators in other countries were able to review products faster. Access to new medicines for U.S. patients lagged behind. For example, a 1989 study by researchers at Tufts University, analyzing differences in the number of new drugs introduced and time to marketing in the United Kingdom compared to the United States for the period 1977 to 1987, found that the United Kingdom led the United States in the number of first introductions of new drugs (114 versus 41) and in the average lead time for mutually available drugs (60.7 months lead time in the United Kingdom versus 28.9 months in the United States) and in the number of exclusively available new drugs (70 versus 54).<sup>1</sup> In addition, a 1992 review of the international literature related to drug lag found that most studies reported the United States, Sweden and Norway to have a long delay in the introduction of new drugs, while the United Kingdom and (West) Germany were generally found to have the shortest delay.<sup>2</sup> Chronic understaffing of drug review and related delays in U.S. patient access to new drugs led to the 1992 enactment of PDUFA. PDUFA provided FDA with added funds that enabled the agency to hire additional reviewers and support staff and upgrade its information technology systems to speed the application review process for new drugs and biological products without compromising FDA's high standards for approval.

Since the beginning of the PDUFA program, there has been a significant improvement in FDA funding for the drug review program, including significant investments in information technology. PDUFA has enabled FDA to virtually double the staff dedicated to the process of reviewing human drug applications since 1992.

Under PDUFA, the industry provides additional funds through user fees that are available to FDA, in addition to appropriated funds, to spend on the human drug review process. Our authority to collect user fees is

“triggered” only when a base amount of appropriated funds, adjusted for inflation, is spent.

In conjunction with PDUFA, FDA set review performance goals that became more stringent each year. These goals applied to the review of original new human drug and biological product applications, resubmissions of original applications, and supplements to approved applications. During the first few years of PDUFA I, we eliminated backlogs of original applications and supplements that had formed in earlier years when the program had fewer resources. Phased in over the 5 years of PDUFA I, the goals were to review and act on 90 percent of priority new drug applications (NDAs), biologics license applications (BLAs), and efficacy supplements (i.e., submissions for products providing significant therapeutic gains) within 6 months of submission of a complete application; to review and act on 90 percent of nonpriority original NDAs, BLAs, and efficacy supplements within 12 months, and on resubmissions and manufacturing supplements within 6 months. Over the course of PDUFA I, we exceeded all of these performance goals.

Under PDUFA II, some review performance goals continued to shorten. For example, by 2002, the PDUFA II goals called on us to review and act on 90 percent of the following:

- Standard new drug and biological product applications and efficacy supplements within 10 months,
- Chemistry and manufacturing control supplements requiring prior FDA approval within 4 months, and
- Class 1 resubmissions (that respond to relatively minor deficiencies such as labeling changes) within 2 months.

In addition, PDUFA II added a new set of goals intended to improve our interactions with industry sponsors during the early years of drug development, again with the goal of making promising new drug therapies available to patients sooner. For example, these procedural goals called for us to meet with sponsors and provide followup meeting minutes within a certain number of days, and provide responses to questions on industry submitted special study protocols within a certain number of days. For example, PDUFA II goals called for us to respond to 90 percent of industry requests:

- Scheduling Type A meetings within 30-calendar days of FDA receipt of the meeting request,
- Scheduling Type B meetings within 60-calendar days of FDA receipt of the meeting request,

- Scheduling Type C meetings within 75-calendar days of FDA receipt of the meeting request, and

- Completing written assessments of the adequacy of special protocols within 45 days of sponsor requests.

However, the agency experienced a much heavier review workload than was accounted for by PDUFA II fee funding. By the end of PDUFA II, the program was beginning to falter in terms of both performance and financial stability. Although we were able to meet the letter of the performance deadlines in many cases, FDA reviewers were not able to allocate time for earlier and more frequent communication and feedback to sponsors that might have resulted in better-quality applications and a higher rate of first-cycle approvals.

Under the current program, reauthorized in 2002 (PDUFA III), additional money from user fees was authorized to better finance the expanded scope and growing volume of demand for FDA review and consultation, and a mechanism was placed in PDUFA to annually adjust fee revenues for increases in workload associated with the process for the review of human drugs. For the first time, PDUFA III also authorized FDA to spend user fee funds on certain aspects of postmarket risk management. The review performance and procedural goals associated with PDUFA III were similar to those under PDUFA II for FY 2002 performance levels, but the PDUFA III program addressed drug safety issues and established several new initiatives to improve application submissions and agency-sponsor interactions during drug development and application review. The goals under PDUFA III included new provisions, for example, to develop guidance for industry on good risk assessment, risk management, and pharmacovigilance practices; to fund outside expert consultants to help evaluate and improve review management processes; and to centralize accountability and funding for all PDUFA information technology initiatives and activities.

Furthermore, in conjunction with PDUFA's reauthorization in 2002, FDA set the goal of creating a guidance for our review staff and industry on good review management principles and practices (GRMPs) as they apply to the first cycle review of NDAs, BLAs, and efficacy supplements. We also set a goal of evaluating whether providing early review of selected applications and additional feedback and advice to sponsors during drug development for selected products can shorten drug development and review times. Two “continuous marketing application”

<sup>1</sup> Kaitin, K.I., N. Mattison, F.K. Northington, L. Lasagna, The drug lag: an update of new drug introductions in the United States and in the United Kingdom, 1977 through 1987, *Clinical Pharmacology and Therapeutics*, 1989; 46 (2):121–38.

<sup>2</sup> Andersson, F., The drug lag issue: the debate seen from an international perspective, *International Journal of Health Services*, 1992; 22(1): 53–72.

(CMA) pilot programs were initiated. CMA Pilot 1 provides for the review of a limited number of presubmitted portions of NDAs and BLAs. Under CMA Pilot 2, FDA and applicants can enter into agreements to engage in frequent scientific feedback and interactions during the investigational new drug phase of product development.

When it enacted PDUFA III, Congress enacted special provisions regarding public accountability in the development of recommendations for PDUFA IV. Congress directed FDA, when developing recommendations to the Congress for PDUFA IV, to "consult with the Committee on Energy and Commerce of the House of Representatives, the Committee on Health, Education, Labor, and Pensions of the Senate, appropriate scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry" (Section 505. Accountability and Reports).

In preparing our proposed recommendations for PDUFA reauthorization, we have conducted technical discussions with regulated industry and have consulted with stakeholders as required by law. We began our public consultation on PDUFA reauthorization with a public meeting held on November 14, 2005 (<http://www.fda.gov/OHRMS/DOCKETS/98fr/05-20875.htm>).

The meeting included presentations by FDA and a series of panels representing different stakeholder groups, including patient advocates, consumer groups, regulated industry, health professionals and academic researchers. The stakeholders were asked to respond to the following questions: (1) What is your assessment of the overall performance of the PDUFA program thus far and (2) What aspects of PDUFA should be retained, or what should be changed, to further strengthen and improve the program?

There was general agreement among the responding stakeholders that PDUFA should be reauthorized. Most expressed the view that drug review should not only include safety and effectiveness review prior to marketing approval, but also should encompass continued safety monitoring after approval. Many panelists supported increased PDUFA funds for postmarket drug safety surveillance, including developing and monitoring risk management tools. A number of panelists also expressed support for increased resources to fund the review of direct-to-consumer (DTC) advertising. Some panelists expressed concern that

over-emphasizing safety might delay patient access to new treatments, and some expressed support for PDUFA funding of "Critical Path" projects to help speed new drug development (see <http://www.fda.gov/oc/initiatives/criticalpath/>).

In addition to our initial public meeting in November 2005, we held followup meetings to obtain further input on the PDUFA program and suggestions regarding what features should be proposed or amended with program reauthorization.

On May 22, 2006, we held a meeting with patient advocacy groups. Overall, these groups supported reauthorization of PDUFA as a vehicle for speeding patient access to safe and effective drug therapies. They also suggested that user fees be increased to sufficiently fund postmarket safety activities and that the issues raised in the March 2006 GAO report entitled, "*Drug Safety: Improvement Needed in FDA's Postmarket Decision-making and Oversight Process*" (GAO-06-402) (<http://www.gao.gov/new.items/d06402.pdf>) report on drug safety be addressed. In addition, it was suggested that FDA establish postmarket performance goals, such as milestones for development of a better postmarket safety system.

On May 23, 2006, FDA held a meeting with consumer advocacy groups to get their input on PDUFA reauthorization. Some consumer groups indicated a preference for full funding of human drug review with appropriated funds rather than user fees, but they generally considered fee-funding to be inevitable and PDUFA reauthorization to be necessary. Given this, the consumer advocacy groups who participated in the meeting emphasized that user fees should be used to enable the agency to adequately cover its priorities, but there should be no ties between user fees and performance goals. They also expressed the view that appropriated funding should be increased and there should be increased funding to enhance FDA's capacity for postmarket safety and DTC advertising review. Some consumer advocates further suggested that FDA charge separate fees for DTC advertising review.

On June 23, 2006, we held a meeting with health professional groups to obtain their views and suggestions for reauthorization. The health professional groups supported PDUFA reauthorization to maintain an efficient process and the availability of safe and effective new drugs on the market. They also thought sufficient funding was needed to maintain a competent scientific staff. The health professional

groups thought PDUFA fees should be increased to support safety surveillance and risk management, and the current statutory time period for using fee funds for safety-related work should be eliminated or expanded. They also felt that fee-funded support for risk management plans should be expanded to include older drugs as well as those recently approved. They indicated that the issues raised in the March 2006 GAO report on drug safety needed to be addressed. Finally, they suggested that PDUFA funds be increased to support the review of DTC advertising.

Congress also directed FDA to publish in the **Federal Register** the proposed recommendations developed through this process after negotiations with the regulated industry, present the proposed recommendations to the congressional committees specified in the statute, hold a public meeting at which the public can present its views on the proposed recommendations, and provide for a period of 30 days for the public to provide written comment on the proposed recommendations.

We have now concluded discussions with industry and other stakeholders regarding reauthorization of PDUFA. The purpose of this document is to publish the recommendations we intend to propose to Congress and announce the dates for the upcoming public meeting and written comment period. After the public meeting and the close of the 30-day comment period, we plan to undertake a careful review of all public comments on these proposed recommendations.

## II. What We Are Proposing to Recommend for PDUFA IV

For PDUFA IV, as described in the following paragraphs, we plan, with a few exceptions, to carry forward the performance goals from PDUFA III and we propose additional goals related to proposed enhancements to the program. Our proposed recommendations fall into three major categories: (1) Proposals to ensure sound financial footing for the human drug review program; (2) proposals to enhance the process for premarket review of human drug applications; and (3) proposals to modernize and transform the postmarket safety system. In addition, we are proposing to recommend a program separate from, but related to, PDUFA pertaining to fees assessed for advisory reviews of DTC television advertisements. The summary table containing the proposals and related fees under PDUFA IV can be found in table 1 of this document. The discussion and additional fee estimates in this section (II) and table 1 of this document,

do not include our proposals and proposed fee revenue figures for review of DTC television advertisements. Those

proposals are provided in section III of this document.

TABLE 1.— PDUFA IV FINANCIAL BASELINE AND ENHANCEMENTS (STARTING IN FY 2008)

Financial Baseline	Dollars	FTE
FY 2007 Baseline—Adjusted for Inflation	\$305,455,400	1539
Inflation Adjustment for FY 2008	\$17,716,600	
Adjustment for Increased Rent and Rent-Related Costs	\$11,721,000	
Adjustment for Increased Work per IND & NDA PDUFA III	\$20,000,000	87
<b>PDUFA IV Baseline Before Enhancements</b>	<b>\$354,893,000</b>	<b>1626</b>
<b>Enhancements</b>		
Premarket—Expediting Drug Development	\$4,600,000	20
Premarket—Improving IT Infrastructure for Drug Review	\$4,000,000	
Postmarket—Modernizing and Transforming Safety System	\$29,290,000	82
<b>PDUFA IV Total<sup>1</sup> (in FY 2008)</b>	<b>\$392,783,000</b>	<b>1728</b>

<sup>1</sup>Further workload adjustment, to account for work levels in FY 2007, is expected to add about \$45,000,000 and 195 FTEs for a final total of about \$437,800,000 and 1923 FTEs for FY 2008.

#### A. Proposed Recommendations to Ensure Sound Financial Footing

Although user fees have provided substantial resources to FDA since the beginning of the program, user fees have not kept up with the increasing costs of the program associated with inflation in pay and benefit costs to the agency, rent and rent-related costs, and workload. Although the current law contains provisions for adjusting fees to reflect the rate of inflation and changes in workload, we found that the statutorily prescribed method for adjusting fees has not adequately accounted for actual growth in costs and workload during PDUFA III. We are proposing changes to the financial provisions of PDUFA to correct for the shortcomings in these adjustment factors and place FDA on a sound financial footing so we can continue with the program and make enhancements to it.

##### 1. Adjustment of Base Fee Revenue Amount for Growth in Cost and Workload

Section 736(b) of the PDUFA provides the basic target fee revenue amounts FDA uses to establish the application, product, and establishment user fees each year. These target fee revenue

amounts are then adjusted for inflation and increases in workload, and the resulting number becomes the amount FDA is authorized to collect in fees. The statutory fee revenue amount for FY 2007 was \$259,000,000. Adjusted for inflation in accordance with PDUFA, that amount became \$305,455,400 for FY 2007. However, the PDUFA IV program will not begin until FY 2008, so it was necessary to further adjust this number to obtain the appropriate target revenues for FY 2008 before any adjustments are made.

FDA's proposed recommendation to Congress resulting from industry discussions is that the base target revenue estimate for FY 2008 should be \$392,783,000 and that this estimate should be further adjusted for workload for FY 2007. FDA would calculate the workload adjustment based on submissions through June 30, 2007, and publish the final amount and supporting calculations when fees for FY 2008 are published. The proposed target revenue estimate for FY 2008 includes the following components:

- The base revenue amount authorized in the current statute for FY 2007, adjusted for inflation using

provisions of the current statute. This amount is \$305,455,400.

- An addition of \$17,716,600 to adjust the base amount for inflation for FY 2008. We assume a continuation of the average FDA payroll and benefit cost inflation of 5.8 percent per year (see the Inflation Adjustment discussion in section II.A.2.a of this document).

- An addition of \$11,721,000 to ensure that fees cover a proportionate share of the increased costs that FDA will have to pay for rent and rent-related costs and one-time costs of the required move to the White Oak facility in Silver Spring, MD. These costs would be added to the fee total to maintain the needed level of review staffing (and associated direct costs) while also paying for these critical nondiscretionary operating costs.

- An addition of \$20,000,000 to adjust the base amount of fee revenues to cover significant increases in FDA's drug review workload that occurred during PDUFA III, but were not captured by the workload adjustment provision of PDUFA III and which we are recommending be revised for PDUFA IV (see the Workload Adjustment discussion in section II.A.2.b of this document). The PDUFA

III workload adjuster captured workload increases associated with increased numbers of submissions, but did not capture workload increases associated with the increased level of effort for each submission. FDA documented that the review effort for each submission increased significantly during PDUFA III. The investigational new drug workload increased markedly because of significantly more meetings per investigational new drug (IND) submitted and because of a sharp increase in the number of special protocol assessments submitted for FDA review.

- An addition of \$37,890,000 to fund the proposed enhancements to the PDUFA program, including enhancements to the premarket review program and proposals for modernizing and transforming the postmarket safety system. The sum of these components yields the proposed target revenue figure of \$392,783,000. (\$392,883,000 = \$305,455,400 + \$17,716,600 + \$11,721,000 + \$20,000,000 + \$37,890,000).

## 2. Proposed Revisions to the Inflation Adjustment and Workload Adjustment Applied to User Fees

(a) *Inflation Adjustment*: The fee revenue amounts for PDUFA III were stated in FY 2003 dollars and the proposed fee revenue amounts for PDUFA IV are stated in FY 2008 dollars. Before fees were assessed each year in PDUFA III, the fee revenue target was increased and compounded based on the higher of either: (1) The CPI/U over the latest 12-month period or (2) the most recent increase in pay for Federal employees in the Washington, D.C. area, compounded since FY 2003. The rate of pay for employees in the Washington D.C. area was higher in all but one year, and the PDUFA III inflation adjustment has resulted in average annual inflation increases of 4.16 percent over each of the last 5 years. However, the actual cost of pay and benefits per full time equivalent (FTE) is increasing faster than this factor. Data from the past 5 years shows that the actual cost of salary and benefits has increased at an average rate of 5.8 percent per year during the past 5 years for FDA. FDA proposes to recommend changing the provision for calculation of the inflation adjustment to add to it a third factor—FDA's actual rate of increase in the costs of pay and benefits per FTE during the most recent 5-year period—and the annual adjustment would be based on the highest of the three factors each year.

(b) *Workload Adjustment*: The workload adjuster currently applied in

PDUFA makes adjustments for changes in numbers of applications, but it is flawed in two ways. First, the surrogate for IND workload in the current workload adjuster is the number of new commercial INDs submitted each year. Since each one of these INDs is active for several years, the number of new applications submitted in any 1 year is a poor surrogate for total IND workload. Second, the workload adjuster does not take into account increases in work associated with active INDs, NDAs, and BLAs. During PDUFA, there has been a substantial increase in the numbers of meetings and special protocol assessments per IND submission. However, the current workload adjuster only takes into consideration changes in numbers of submissions—not additional activity required per submission. Since FY 2002, the number of meetings per commercial IND has increased by close to 30 percent, and the number of special protocol assessments is up over 90 percent. This same phenomenon occurs with NDAs as well, but to a somewhat lesser extent.

To remedy these flaws, the following changes are proposed: First, we recommend changing the surrogate for IND workload in the statute from the numbers of new commercial INDs received each year to the total number of active commercial INDs each year. Active INDs are those that have had at least one submission in the previous 12-month period. Second, we recommend using an adjuster applied to the numbers of NDA/BLAs and INDs. The proposed adjuster would adjust the numbers of these applications in proportion to the impact on workload of increased meetings and special protocol adjustments for INDs and for increased meetings, labeling supplements, and annual reports for NDAs and BLAs.

Under the proposed change to the workload adjuster, we also propose to contract with an independent accounting firm to examine the new adjuster and make recommendations, if needed, for further improving this adjuster.

## 3. Technical Changes to Increase Administrative Efficiency of the User Fee Program

The FDA is proposing to recommend several technical changes to PDUFA to simplify some of FDA's current procedures, to clarify the original intent of several PDUFA definitions, and to remove potential ambiguity. FDA's analysis of the impact of these changes indicates that they would be revenue-neutral and would have a minimal impact on industry fee-payers. These

technical proposals include the following:

(a) Simplify the definition of "human drug application" to include all new drug applications under section 505(b) of the Federal Food, Drug, and Cosmetic Act;

(b) Amend the definition of "small business" for the purpose of fee collection to reinstate language from the original PDUFA statute that specifies that to qualify as a small business, the company may not have an approved product already introduced in or delivered for introduction into interstate commerce;

(c) Include capsules, tablets, and lyophilized products as examples in the definition of final dosage form to provide clarification of what constitutes a finished dosage form;

(d) Revise the waiver provisions to clarify that the person named as the applicant and assessed the user fee is the person who is eligible to request a waiver or reduction of fees;

(e) Change the date for the calculation of the adjustment factor so it can be calculated before the President's budget goes to Congress;

(f) Clarify that for fee purposes, applications withdrawn before filing will be treated as applications that FDA refuses to file, and that they will be assessed a full fee if filed again or filed over protest;

(g) For user fee purposes, reinstate the definition of "person" to include affiliates, as enacted under FDAMA

(h) Delay offsets for collections in excess of appropriations in any year to the final year of the PDUFA program and make offsetting reductions only if cumulative fees collected over the first 4 years exceed cumulative appropriations for fees over the same period; and

(i) Revise the definition of "prescription drug product" for the purpose of fee collection, to clarify the exclusion of products on discontinued product lists maintained by Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

## B. Enhancing the Process for Premarket Review

In the premarket review area, several changes were made in PDUFA III as compared to PDUFA II. These are outlined as follows:

- *Continuous marketing application pilot programs*: Two pilot programs were established under PDUFA III to test whether providing early review of selected applications and additional feedback and advice to sponsors during drug development for selected products

can further shorten drug development and review times. Pilot 1 involved a commitment on the part of FDA to review and provide feedback to the sponsor within 6 months of submission of “reviewable units” of an application in advance of the submission of the complete application. This pilot program represented an extension of the “rolling review” program begun under FDAMA and was limited to applications that had received a Fast Track designation. Pilot 2 involved a commitment on the part of FDA to provide more structured and extensive interaction and feedback to sponsors for up to one Fast Track application per review division during drug development. This pilot represented an extension of the usual interactions between FDA and sponsors during drug development. To evaluate the costs and benefits of these pilots, FDA commissioned an independent assessment. The CMA Pilot 1 Evaluation and Pilot 2 Preliminary Evaluation Studies—Final Report is available on the FDA Web site at <http://www.fda.gov/ope/CMA/CMAFinalReport.pdf>. After review of the findings, FDA and industry representatives have agreed that although the pilots demonstrated value in some areas, the overall added benefits of the programs did not justify their costs to FDA. Therefore, FDA is proposing to recommend that the CMA pilot programs will not be continued in PDUFA IV.

- *First cycle review performance:* In PDUFA III, FDA committed to several new goals that were focused on improving the effectiveness and efficiency of first cycle reviews in an attempt to decrease the number of multi-cycle reviews without compromising FDA’s traditional high standards for approval. The first new goal was for FDA to notify the applicant of any substantive deficiencies identified in an application during the initial filing review. The identification of such deficiencies was to be communicated to the applicant within 14 days of the 60-day application filing date, which is commonly known as a “74 day letter.” FDA has consistently met or exceeded the goals for communication of these early deficiencies. The second new goal was for FDA to develop and publish a final joint CDER/CBER guidance on GRMPs. FDA published a final GRMP final guidance on March 30, 2005, entitled, “*Guidance for Review Staff and Industry on Good Review Management Principles and Practices for Prescription Drug User Fee Act Products; Availability*,” at <http://www.fda.gov/>

[OHRMS/DOCKETS/98fr/05-6404.htm](http://www.fda.gov/OHRMS/DOCKETS/98fr/05-6404.htm) (70 FR 16507; March 31, 2005). As part of the goals, FDA also committed to develop and implement a training program for all CDER and CBER review staff on the GRMPs. FDA met the goal for training all review staff on the GRMPs and has incorporated training on the guidance as part of new reviewer training. Finally, FDA committed to commission an independent consultant evaluation of the factors associated with the conduct of first cycle reviews. The first study was a retrospective analysis of first cycle reviews for NME and original BLAs submitted in FY2002–2004, and is available on the FDA Web site at <http://www.fda.gov/ope/pdufa/PDUFA1stCycle/pdufa1stcycle.pdf>. The second study was a prospective study of first cycle reviews for NME and original BLA submissions starting in FY05 and continuing through FY07, and is currently in progress. FDA is proposing to recommend the continuation of first cycle review performance initiatives.

- *Independent consultants for biotechnology clinical trial protocols:* This initiative allowed applicants for certain biotechnology products to request that FDA engage an independent expert consultant, selected by FDA, to participate in the agency’s review of the protocol for clinical studies that were expected to serve as the primary basis for a claim. FDA has received no requests under this initiative during PDUFA III and, after discussions with industry representatives, FDA is proposing not to include this initiative in the recommended PDUFA IV program.

#### 1. Proposed Recommendations for Enhancement of Premarket Review Process

In the area of premarket review, FDA is proposing to recommend enhancements in two areas: (1) Good review management principles and (2) expediting drug development.

(a) *Expanding Implementation of GRMPs:* In the area of GRMPs, we are proposing to recommend further enhancements associated with notifying applicants at the time of the “74-day letter” of the anticipated timeline for review of the application, including the anticipated date for initiation of discussions regarding product labeling and any FDA requests for postmarketing study commitments (PMCs).

Historically, labeling discussions have been initiated at the late stages of a review, often in the last week before approval. Similarly, the agency often communicates requests for postmarketing commitments late in the review cycle. Initiation of discussion of

these important elements of the review of an application late in the review cycle is often due to the inability of FDA to complete its review of the application earlier because of an imbalance between workload and available review staff time. Late initiation of these important discussions is not consistent with the best practices that FDA has identified and published in the GRMP guidance.

An understanding on the part of both the reviewers and the applicant of the process and timeline for the review would facilitate an efficient and scientifically sound review. FDA believes that adhering to a timeline that includes earlier initiation of discussion of labeling, coupled with the new physician labeling regulations (see *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products* at <http://www.fda.gov/OHRMS/DOCKETS/98fr/06-545.pdf>) (71 FR 3922, January 24, 2006), would result in clearer, more readily understandable labeling for new products. Furthermore, FDA believes that initiation of discussions of possible postmarketing commitments earlier in the process would allow for the commitments to be more focused on the data needed to further inform the best use of the products. We also expect that earlier discussion of PMCs would help to ensure that the agreed to studies and study schedules are feasible, thereby improving the timely completion of the studies by the applicant.

The proposed recommendations under the enhancements for GRMP are also intended to encourage applicants to provide FDA with applications that are complete for review at the time of submission. The submission of complete applications would allow FDA to effectively manage and adhere to its review schedule and, ultimately, may result in faster access to these new products without any compromise to FDA’s traditional high standards for approval. Consequently, FDA believes these proposed recommendations to be in the best interest of the agency, the applicant, and, ultimately, the public health.

(b) *Expediting drug development:* One of the things that the agency can do to enhance the development of new and beneficial drugs is to provide guidance to industry to clarify current agency thinking on a variety of topics including, among other things, clinical trial design. Our experience and insight, gained through years of review, can help the industry avoid wasting scarce research and development resources on clinical trials that are not likely to produce results because of flawed designs. By clarifying the agency’s

expectations regarding the nature of data needed to support certain types of claims, we can allow the industry to focus their efforts on useful trials and decrease less useful experimentation. This would have the benefit of decreasing exposure of subjects to unapproved products, decreasing the amount of time required to bring a beneficial new drug to market, and, possibly, decreasing the total cost of bringing the new drug to market, which should translate to lower drug prices for the consumer.

Guidance development by the agency requires substantial time commitments from those who are already heavily involved in the review effort. The PDUFA IV proposal includes increased user fees that would be used to fund additional staff resources to develop the following guidances to enhance clinical drug development (the FY dates for each guidance represent FDA's proposed commitment to publish a draft guidance on that topic by no later than the end of FY listed):

1. **Clinical Hepatotoxicity—FY 2008.** This guidance would address how to evaluate a drug for possible hepatotoxicity during drug development and how FDA will review an application to look for signs that a drug may be a significant hepatotoxin.

2. **Non-inferiority Trials—FY 2008.** This guidance would describe FDA's perspective on the design of noninferiority trials. Topics addressed are expected to include how to select the active control, how to document the effect size of the active control versus placebo, and how to establish the noninferiority margin of interest.

3. **Adaptive Trial Designs—FY 2008.** This guidance would explain FDA's perspective on the use of adaptive trial designs during drug development. Topics to be addressed include the definition of adaptive trial designs, recommended designs, and how the statistical issues should be addressed in analyzing trials.

4. **End of Phase 2(a) Meetings—FY 2008.** This guidance would outline the procedures and data needed for an end-of-phase 2a (EOP2a) meeting. The EOP2a meetings are intended to facilitate FDA interactions with a sponsor earlier in the design of the development program to maximize the value of the phase 2 program with the overall goal of making drug development more efficient and effective.

5. **Multiple Endpoints in Clinical Trials—FY 2009.** This guidance would describe FDA's perspective on the appropriate procedures and analyses for trials with multiple endpoints (e.g., a

trial with multiple co-primary endpoints).

6. **Enriched Trial Designs—FY 2010.** This guidance would focus on approaches to enrich the clinical trial population to better define the efficacy or safety of the drug under development.

7. **Imaging Standards for Use as an End Point in Clinical Trials—FY 2011.** This guidance would focus on the use of images as important endpoints in controlled clinical trials. Issues would include image acquisition, archiving, and blinded reading.

The commitment, under this part of the proposed PDUFA IV program, would allow us to pursue the development and publication of several guidance documents to facilitate the development of new, life-saving therapies, moving them more efficiently from the laboratory to the bedside.

In addition to funding the development of guidances, under PDUFA IV we are proposing to collect user fees to hire additional staff to free up reviewer time to enable greater participation in scientific research collaborations that will ultimately help clarify regulatory pathways for new technologies and potential new biomarkers for drug safety and effectiveness. For example, FDA intends to participate in workshops with representatives from the scientific community (including industry, academia, and other interested stakeholders) to further the science toward development of guidance documents in the following areas:

1. **Predictive toxicology—Emerging science** such as toxicogenomics, proteomics, metabolomics, and molecular imaging, is expected to yield more sensitive, specific, and informative tests for drug organ toxicity than the toxicology screening techniques currently in use. FDA reviewers will need to participate extensively in the design of studies intended to qualify these new safety tests for regulatory uses.

2. **Biomarker Qualification—**Biomarkers are frequently used during drug development to understand the effect of a drug on biologic systems and to predict clinical response. Before biomarkers can be used for regulatory decision making they must be qualified. FDA expertise will be needed on an ongoing basis in the effort to select and test candidate biomarkers for qualification. FDA reviewers will need to participate in the design of the definitive studies intended to qualify the biomarker for a specific regulatory use.

3. **Missing Data—**In controlled clinical trials it is often impossible to ensure that every data element described in the protocol is collected for every study subject. For example, subjects often discontinue participation in a trial early and do not return for further study visits. The question of how to handle missing data when analyzing the results of a trial is a very complex one, and FDA would expect to work in collaboration with outside stakeholders to further explore the science of this issue and develop appropriate procedures.

Finally, under the proposal for PDUFA IV, user fees would be used to support FDA participation in workshops and other public meetings to explore new approaches to a structured model for benefit/risk assessment. The results of these interactions would be used to assess whether pilot(s) of such new approaches can be conducted during PDUFA IV. These efforts may lead to the development of guidance documents. Under PDUFA IV, FDA proposes to collect an additional \$4,600,000 in FY 2008 and, in subsequent years, adjusted for inflation and workload, to support at least 20 FTEs to engage in the collaborations with outside stakeholders described previously.

2. **Improving the IT Infrastructure for Human Drug Review**

Under PDUFA III, we agreed to certain performance goals associated with better management of information technology (IT) resources and improved consistency of IT practices across the human drug review program. Under PDUFA III, we centralized accountability for PDUFA IT funding under the Chief Information Officer (CIO); established an IT Project Management Office to develop and implement processes policies, based on the Capability Maturity Model Integration process improvement approach to improve software development practices; implemented the electronic Common Technical Document standard for electronic regulatory submissions; established a common secure single point of entry for the receipt and processing of all electronic submissions, commonly called the FDA Electronic Submissions Gateway; and established a common approach to managing desktop hardware and software configurations. We are now in the process of establishing a common approach for secure e-mail that will be implemented throughout the PDUFA program. Following provisions in the PDUFA III commitment letter, we have also met quarterly with industry representatives to discuss progress

towards these IT goals and to address technical implementation issues. These accomplishments have built a strong foundation for further progress toward an IT environment that better serves the human drug review program.

Under PDUFA IV, we recommend collection of an additional \$4,000,000 annually, starting in FY 2008 to enable the agency to commit to several IT performance goals that would move FDA and industry towards an all-electronic environment, which would increase the efficiency of the review process. Under these proposed goals, we would commit to develop a 5-year IT plan that would lay out the technical approach for achieving a more integrated, standards-based electronic regulatory submission and review environment. The plan would help FDA, industry, and stakeholders make related IT investments in a more coordinated manner. By the end of PDUFA IV, following implementation of these proposed goals, human drug application sponsors would be able to send in their electronic applications with automated cross-links to previously submitted data and information, so that they only have to submit things once. In addition, FDA reviewers would be able to retrieve all relevant submissions and related data electronically from their work stations and would have efficient tools for searching and analyzing data to support their reviews. These capabilities would enable more efficient and reliable management of regulatory submissions.

By the end of PDUFA IV, if resources are provided as expected, we intend to have the capability to handle two-way transmission of regulatory correspondence with industry, which would accelerate the movement toward an all-electronic submission and review environment.

To determine whether we are moving towards achieving the IT goals described in PDUFA IV, we further propose to track several key performance indicators of the adoption rate of electronic submissions and the technical error rates associated with those submissions, so that we can more closely monitor progress toward the all-electronic environment.

Finally, in the recommended IT performance goals for PDUFA IV, we propose a cost-effective approach that minimizes expenditures on existing legacy systems and redirects those funds toward the development of new common systems that are better coordinated and more flexible.

### *C. Modernizing and Transforming the Postmarket Drug Safety System*

In PDUFA III, for the first time, FDA was authorized to spend user fees revenues to fund improvements in drug safety. This change provided important new resources to help improve postmarket safety but our experience has shown that further improvements can be achieved. The definition of the "process for the review of human drug applications" in section 735 of PDUFA describes which products PDUFA funds can be used for in terms of postmarket safety review as well as the length of time after product approval PDUFA funds can be used for such safety review. Specifically, 735(6)(F) states: "In the case of drugs approved after October 1, 2002, under human drug applications or supplements: collecting, developing, and reviewing safety information on the drugs, including adverse event reports, during a period of time after approval of such applications or supplements, not to exceed three years."

In addition, the PDUFA III Reauthorization Performance Goals and Procedures document stated that user fees may be used "for a period of up to two years post-approval for most products and for a period of up to three years for products that require risk management beyond standard labeling \* \* \*." The stated purpose of this language was to provide user fees to review an applicant's implementation of risk management plans for this period of time and to allow for evaluation of study reports, product use, and other safety activities. Drug safety activities outside of the specified timeframe were to be funded with appropriated dollars.

As part of the PDUFA IV program, we propose to recommend further enhancing the program by removing the language that limits the spending of user fees outside of the specified timeframe. Current data show that safety issues can arise after a drug has been on the market for 8 or more years. A recent FDA analysis of safety-related label changes made between October 2002 and August 2005, for all drug products with a labeling change, found that the total number of safety-related label changes exceeded 160 changes for drugs 3 years postapproval and remained at or above that high level until 8 years postapproval before starting to decline. All stakeholders agree that the current limitations on use of funds for postmarketing safety-related activities present an opportunity for improving the agency's ability to optimally support adverse event surveillance, detection, evaluation, and management. Enhancing

the program by eliminating such limitations would help both FDA and drug sponsors because safety assessments of drug products by both FDA and sponsors are necessary for drugs over time to adequately manage risks, regardless of approval date. Increased resources, including from PDUFA funds, would enable FDA to engage in safety review activities, such as studies of drugs in the same class approved before and after October 1, 2002, to adequately assess significant drug safety issues. The current description of postmarketing safety activities in the definition of the "process for the review of human drug applications" could also be revised to better reflect the broad variety of activities that are important to postmarket safety review.

As part of the reauthorization of PDUFA, FDA proposes changing the statute to eliminate the statutory restrictions so that PDUFA fees could be used to assess safety issues postapproval, independent of a product's approval date and would allow the agency to review the drug's safety in whatever time frame risks arise using all available resources. This change would provide much needed support for timely, predictable, consistent, and scientifically sound regulatory decisionmaking and would work towards a fully integrated evaluation of drugs and biologics throughout their life cycle.

In addition, we propose expanding the description of postmarket safety activities to capture a broader range of activities related to postmarket safety review. For example, FDA would use \$29,290,000 in new user fee funds to enhance and modernize the current U.S. drug safety system. We would adopt new scientific approaches, improve the utility of existing tools for the detection, evaluation, prevention, and mitigation of adverse events associated with drugs and biological products. In addition, FDA would use these funds to continue to enhance and improve communication and coordination between pre- and postmarket review staff. Potential activities in this area might include integration of certain proposed recommendations made by the Institute of Medicine (IOM) in their September 2006 report entitled, "*The Future of Drug Safety: Promoting and Protecting the Health of the Public.*"

PDUFA IV funds would also be used to support a number of activities designed to modernize the process of pharmacovigilance. One key initiative would be the implementation of an FDA contract to one or more outside research organization(s) to conduct research on

determining the best way to maximize the public health benefits associated with collecting and reporting serious and nonserious adverse events occurring throughout a product's life cycle. Studies under this contract would answer such central questions as the number and types of safety concerns that are discovered by various types of adverse event collection, the age of the medical products at the time such safety concerns are detected, and the types of actions that are subsequently taken and their ultimate effect on patient safety.

PDUFA IV funds would also support the development of a guidance document to delineate epidemiology best practices. Epidemiologic studies using large automated databases are increasingly being performed to evaluate drug safety. These studies and safety analyses are complex and employ a variety of nonstandardized analytic methods and assumptions. During the course of PDUFA IV, FDA, with input from academia, industry, and others from the general public, would hold a public workshop to identify best practices in this emerging field, ultimately developing a document that addresses epidemiology best practices and provides guidance on how to carry out scientifically sound observational studies using quality data resources.

Another critical part of the transformation of the drug safety program would be maximizing the usefulness of tools used for adverse event detection and risk assessment. To achieve this end, data other than spontaneous adverse event reports, including population-based epidemiological data and other types of observational data resources, would be used and evaluated. Access to these types of data would expand our capability to carry out targeted postmarketing surveillance, look at class effects of drugs, and potentially carry out signal detection using data resources other than reports from FDA's adverse event reporting system (AERS). PDUFA IV funds would be used to obtain access to additional databases and increase program staffing with epidemiologists, safety evaluators, and programmers who can use these new resources.

As mentioned previously, the PDUFA III Reauthorization Performance Goals and Procedures document provided user fees to review implementation of a risk management plans for a limited period of time and to allow for evaluation of study reports, product use, and other safety activities. Risk communication and management have now become a routine part of human drug review, yet many of the risk management and risk communication tools the industry uses

remain unproven and unstandardized. To promote more effective and consistent use of these tools to mitigate the risk of drugs and biological products, under PDUFA IV, with input from academia, industry, and others from the general public, we would conduct an annual systematic public discussion and review of the effectiveness of one to two risk management programs and one major risk management tool per year. Reports from these discussions would be posted on the FDA Web site.

FDA would also use PDUFA IV fees to enhance the agency's AERS and surveillance tools, to strengthen its IT infrastructure to support access and analyses of externally linked databases, and to support a safety workflow tracking system. This support for drug and biological product safety-related IT systems is critical to ensure the best collection, evaluation, and management of the vast quantity of safety data received by FDA.

FDA would use PDUFA IV funds to develop and periodically update a 5-year plan describing the range of activities designed to enhance and modernize the drug safety system. FDA would publish and seek public comment on an initial plan for these activities and conduct an annual assessment of progress against the plan to be published on FDA Web site. In addition to progress against the specific modernization activities described previously, the annual report would include an update on FDA efforts to facilitate the interactions between the Office of New Drugs and the Office of Surveillance and Epidemiology related to the process of evaluating and responding to postmarketing drugs safety/adverse event reports. FDA would publish updates to the modernization plan as FDA deems necessary and post on FDA's Web site draft revisions to the plan, soliciting comments from the public on those draft revisions and then carefully considering all public comments before completing and publishing updates to the plan.

Another recent study by the IOM, entitled "*Preventing Medication Errors: Quality Chasm Series*," (July 20, 2006), estimates that, on average, every hospitalized patient is subject to at least one medication error per day. These errors lead to costly morbidity and mortality. The IOM concluded that drug names that look or sound similar, in addition to the layout and presentation of important drug information on the label, labeling, and packaging of drug products increase the risk of medication errors. The IOM report recommended

that the FDA, the pharmaceutical industry, and other stakeholders should collaborate in several areas to improve methods for naming and labeling drug products and communicating medication information to providers and consumers and advised the FDA to develop guidance documents for industry related to drug naming, labeling, and packaging.

Using PDUFA IV funds, FDA would implement various measures to reduce medication errors related to look-alike and sound-alike proprietary names as well as factors such as unclear label abbreviations, acronyms, dose designations, and error-prone label and packaging designs. Activities to be funded include guidance development, review performance goals, and initiation of a pilot program to explore a different paradigm for proprietary name review.

Fees would provide the resources FDA needs to publish three guidances to industry: (1) Guidance on the contents of a complete submission package for a proposed proprietary drug/biological product name; (2) guidance on best practices for naming, labeling, and packaging drugs and biologics to reduce medication errors; and (3) guidance on proprietary name evaluation best practices. These guidances, developed after consultation with industry, academia, and others from the general public, would provide a scientifically sound and consistent approach to the selection, evaluation, and review of proprietary names and would also create a framework for best practices for the layout and design of drug labels and packaging to prevent or minimize medication errors.

In addition, under the proposed PDUFA IV program, FDA would commit to a performance goal of 180 days for reviewing proprietary names submitted during the IND and NDA phases. For submissions received as part of an IND, submitted as early as the end of phase 2 of drug development, FDA would increase the percentage of submissions subject to this goal, from 50 percent in year 1 to 90 percent in year 4 of the program. In a similar phased-in fashion, for submissions received as part of an NDA or BLA, FDA would review 50 percent (in year 1) increasing to 90 percent (in year 4) of proprietary name submissions within 90 days of receipt. Commitment to review goals would enhance the timeliness and predictability of proprietary name review.

During PDUFA IV, FDA proposes to develop and implement a pilot program that shifts the responsibility for testing proposed proprietary names from FDA to the pharmaceutical industry. This

program would enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names and submit the data generated from those evaluations to FDA for review prior to approval. Using this more traditional FDA review role was recommended by the IOM in November 1999 report, entitled “*To Err Is Human: Building a Safer Health System,*” as well as the HHS Advisory Committee on Regulatory Reform in November of 2002 Secretary’s Advisory Committee on Regulatory Reform, November 21, 2002, [http://regreform.hhs.gov/meetinginfo/november\\_meetinginfo.htm](http://regreform.hhs.gov/meetinginfo/november_meetinginfo.htm). The proposed pilot would allow this approach to be evaluated for its contribution to the efficiency and timeliness of proprietary name review.

**III. What We Are Proposing to Recommend for Review of Direct-To-Consumer Advertising**

In addition to our proposed recommendations for enhancements to the current human drug review program, we are proposing to recommend a program separate from, but related to, PFUFA assessing fees for advisory reviews of DTC television advertisements. Research has shown

there can be benefits associated with DTC prescription drug television advertising, such as informing patients about the availability of new treatment options and encouraging patients to see a physician about an illness for the first time. Notwithstanding these benefits, concerns have arisen about the effects of DTC television advertisements on prescribing practices and prescription drug use. Companies have the option of submitting their proposed advertisements to FDA for advisory review before publicly disseminating them, which gives them with the benefit of FDA input on whether or not the advertisements are accurate, balanced, and adequately supported, enabling them to address any problems before the advertisements are shown to the public, thus improving the quality of the advertisements.

Companies recognize the benefits this advisory review mechanism offers. In fact, PhRMA recently stated in its voluntary guidance principles on DTC advertising that companies should submit all new DTC television advertisements to FDA before broadcasting them <http://www.phrma.org/files/>

*DTCGuidingprinciples.pdf*. However, although FDA’s DTC advisory review workload has been steadily increasing, staffing for this activity has remained level. As a result, it is impossible for FDA to review all of the DTC television advertisement advisory submissions it receives in a timely manner. The lack of timely, predictable FDA review times for DTC television advertisements is detrimental to companies’ ability to accurately set timeframes for their marketing campaigns and discourages companies from submitting these materials for advisory review.

We propose creating a separate program, not directly included under PDUFA IV, to assess, collect, and use fees for the advisory review of prescription drug television advertisements. These user fees would not be funded by application, product, or establishment fees assessed under PDUFA. Instead, these new fees would be assessed separately and collected only from those companies that intend to seek FDA advisory reviews of DTC television advertisements. The proposed recommendation for fee funding and the estimated number of supported staff are summarized in table 2 of this document.

TABLE 2.—PROPOSED FEES FOR DTC ADVERTISEMENT REVIEW (STARTING IN FY 2008)

Proposed Program	Dollars	FTE
Advisory Review of DTC Television Advertisements	\$6,250,000	27
<b>Program Total (in FY 2008)</b>	<b>\$6,250,000</b>	<b>27</b>

This program would provide for increased FDA resources to allow for the timely review of DTC television advertisement advisory submissions. To ensure stable funding for the program in case the number of advisory submissions fluctuates widely from year to year, the program would assess a one-time participation fee. The program would then charge fees each year for each advisory review requested. These new fees would provide sufficient resources for FDA to hire additional staff to review DTC television advisory submissions in a predictable, timely manner. FDA anticipates collecting \$6.25 million in annual fees during the first year of the program (and a similar amount to go into the reserve fund) to support 27 additional staff to review DTC television advertising. Advisory review fee amounts would be adjusted annually for inflation and to take into account increases in workload. As part

of this program, FDA is proposing to commit to certain performance goals including review of a certain number of original advisory review submissions in 45 days and resubmissions in 30 days. The goals would be phased in over the 5 years of the program to allow for recruitment and training of staff.

**IV. What Information Should You Know About the Meeting?**

*A. When and Where Will the Meeting Occur? What Format Will We Use?*

Through this document, we are announcing the convening of a public meeting to hear stakeholder views on the recommendations we propose to provide to Congress on the reauthorization of PDUFA IV.

We will conduct the meeting on February 16, 2007, at the Grand Hyatt Washington at Washington Center (see **ADDRESSES**). In general, the meeting format will include presentations by

FDA and a series of panels representing different stakeholder interest groups (such as patient advocates, consumer advocates, industry, health professionals, and academic researchers). We will also give individuals the opportunity to make presentations at the meeting, and for organizations and individuals to submit written comments to the docket after the meeting.

*B. How Do You Register for the Meeting or Submit Comments?*

If you wish to attend and/or make a presentation at the meeting, please send an electronic mail message to [CBERTrainingSuggestions@fda.hhs.gov](mailto:CBERTrainingSuggestions@fda.hhs.gov) by February 2, 2007. Your e-mail should include the following information: Name, Company, Company Address, Company Phone Number, and E-mail Address. You will receive a confirmation within 2 business days.

We also will accept walk-in registration at the meeting site, but space is limited, and we will close registration when maximum seating capacity (approximately 500) is reached.

We will try to accommodate all persons who wish to make a presentation. The time allotted for presentations may depend on the number of persons who wish to speak.

Additionally, regardless of whether you wish to make a presentation or simply attend the meeting, please notify us if you need any special accommodations (such as wheelchair access or a sign language interpreter).

If you would like to submit comments regarding these proposed recommendations, please send your comments to the Division of Dockets Management (see **ADDRESSES**). Submit a single copy of electronic comments or two paper copies of any written comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

To ensure consideration of your comments, you should send your comments no later than February 23, 2007.

#### *C. Will Meeting Transcripts Be Available?*

We will prepare a meeting transcript and make it available on our Web site ([www.fda.gov](http://www.fda.gov)) after the meeting. We anticipate that transcripts will be available approximately 30 business days after the meeting. The transcript will also be available for public examination at the Division of Dockets Management (HFA-305), 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m. Monday through Friday.

Dated: January 10, 2007.

#### **Jeffrey Shuren,**

*Assistant Commissioner for Policy.*

[FR Doc. 07-122 Filed 1-11-07; 8:45 am]

**BILLING CODE 4160-01-S**

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **Substance Abuse and Mental Health Services Administration**

#### **Current List of Laboratories Which Meet Minimum Standards To Engage in Urine Drug Testing for Federal Agencies**

**AGENCY:** Substance Abuse and Mental Health Services Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Department of Health and Human Services (HHS) notifies Federal agencies of the laboratories currently certified to meet the standards of Subpart C of the Mandatory Guidelines for Federal Workplace Drug Testing Programs (Mandatory Guidelines). The Mandatory Guidelines were first published in the **Federal Register** on April 11, 1988 (53 FR 11970), and subsequently revised in the **Federal Register** on June 9, 1994 (59 FR 29908), on September 30, 1997 (62 FR 51118), and on April 13, 2004 (69 FR 19644).

A notice listing all currently certified laboratories is published in the **Federal Register** during the first week of each month. If any laboratory's certification is suspended or revoked, the laboratory will be omitted from subsequent lists until such time as it is restored to full certification under the Mandatory Guidelines.

If any laboratory has withdrawn from the HHS National Laboratory Certification Program (NLCP) during the past month, it will be listed at the end, and will be omitted from the monthly listing thereafter.

This notice is also available on the Internet at <http://workplace.samhsa.gov> and <http://www.drugfreeworkplace.gov>.

**FOR FURTHER INFORMATION CONTACT:** Mrs. Giselle Hersh or Dr. Walter Vogl, Division of Workplace Programs, SAMHSA/CSAP, Room 2-1035, 1 Choke Cherry Road, Rockville, Maryland 20857; 240-276-2600 (voice), 240-276-2610 (fax).

**SUPPLEMENTARY INFORMATION:** The Mandatory Guidelines were developed in accordance with Executive Order 12564 and section 503 of Public Law 100-71. Subpart C of the Mandatory Guidelines, "Certification of Laboratories Engaged in Urine Drug Testing for Federal Agencies," sets strict standards that laboratories must meet in order to conduct drug and specimen validity tests on urine specimens for Federal agencies. To become certified, an applicant laboratory must undergo three rounds of performance testing plus an on-site inspection. To maintain that

certification, a laboratory must participate in a quarterly performance testing program plus undergo periodic, on-site inspections.

Laboratories which claim to be in the applicant stage of certification are not to be considered as meeting the minimum requirements described in the HHS Mandatory Guidelines. A laboratory must have its letter of certification from HHS/SAMHSA (formerly: HHS/NIDA) which attests that it has met minimum standards.

In accordance with Subpart C of the Mandatory Guidelines dated April 13, 2004 (69 FR 19644), the following laboratories meet the minimum standards to conduct drug and specimen validity tests on urine specimens:

ACL Laboratories, 8901 W. Lincoln Ave., West Allis, WI 53227, 414-328-7840 / 800-877-7016 (Formerly: Bayshore Clinical Laboratory).

ACM Medical Laboratory, Inc., 160 Elmgrove Park, Rochester, NY 14624, 585-429-2264.

Advanced Toxicology Network, 3560 Air Center Cove, Suite 101, Memphis, TN 38118, 901-794-5770 / 888-290-1150.

Aegis Analytical Laboratories, Inc., 345 Hill Ave., Nashville, TN 37210, 615-255-2400.

Baptist Medical Center-Toxicology Laboratory, 9601 I-630, Exit 7, Little Rock, AR 72205-7299, 501-202-2783 (Formerly: Forensic Toxicology Laboratory Baptist Medical Center).

Clinical Reference Lab, 8433 Quivira Road, Lenexa, KS 66215-2802, 800-445-6917.

Diagnostic Services, Inc., dba DSI, 12700 Westlinks Drive, Fort Myers, FL 33913, 239-561-8200 / 800-735-5416.

Doctors Laboratory, Inc., 2906 Julia Drive, Valdosta, GA 31602, 229-671-2281.

DrugScan, Inc., P.O. Box 2969, 1119 Mearns Road, Warminster, PA 18974, 215-674-9310.

Dynacare Kasper Medical Laboratories\*, 10150-102 St., Suite 200, Edmonton, Alberta, Canada T5J 5E2, 780-451-3702 / 800-661-9876.

ElSohly Laboratories, Inc., 5 Industrial Park Drive, Oxford, MS 38655, 662-236-2609.

Gamma-Dynacare Medical Laboratories\*, A Division of the Gamma-Dynacare Laboratory Partnership, 245 Pall Mall Street, London, ONT, Canada N6A 1P4, 519-679-1630.

Kroll Laboratory Specialists, Inc., 1111 Newton St., Gretna, LA 70053, 504-361-8989 / 800-433-3823 (Formerly: Laboratory Specialists, Inc.).