

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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Display Date	11-15-01 @
Publication Date	11-19-01
Certifier	S. Reese

4:39 pm

[Docket No. 01 N-04501

Prescription Drug User Fee Act (PDUFA); Public Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing a public meeting on the Prescription Drug User Fee Act (PDUFA). The legislative authority for PDUFA expires at the end of September 2002, and without further legislation the fees and resources provided under PDUFA will also expire. FDA is now evaluating the PDUFA provisions. The Federal Food, Drug, and Cosmetic Act (the act) encourages FDA to consult with stakeholders, as appropriate, in carrying out agency responsibilities. Accordingly, FDA will convene a public meeting to hear stakeholder views on this subject. FDA is proposing three specific questions, and the agency is interested in responses to these questions and any other pertinent information stakeholders would like to share.

*Date and Time:* The public meeting will be held on Friday, December 7, 2001, from 9 a.m. to 5 p.m. Registration to attend the meeting must be received by November 30, 2001. Submit written or electronic comments by January 25, 2002.

*Location:* The public meeting will be held at the Hyatt Regency Bethesda, One Bethesda Metro Center, Bethesda, MD 20814.

*For information regarding this notice contact:* Patricia A. Alexander, Office of Consumer Affairs, Office of Communications and Constituent Relations (HFE-40), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4391, FAX 301-827-3052,

e-mail: palexand@oc.fda.gov.  
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*For registration information contact:* Carole A. Williams, Office of Consumer Affairs, Office of Communications and Constituent Relations (HFE-40), Food and Drug Administration, Rockville, MD 20857, 301-827-4394, FAX 301-827-2866, e-mail: [pubmtg@oc.fda.gov](mailto:pubmtg@oc.fda.gov). All registration materials should be sent to Carole A. Williams. Electronic registration for this meeting is available at: <http://www.accessdata.fda.gov/scripts/oc/dockets/meetings/meetingdockets.cfm>. Registrations will be accepted on a first-come, first-served basis. Individuals who register to make an oral presentation will be notified of the scheduled time for their presentation prior to the meeting. All participants are encouraged to attend the entire day.

*Registration and Requests for Oral Presentation:* To register to attend the meeting, submit your name, title, business affiliation, address, telephone, fax number, and e-mail address. If you wish to make an oral presentation during the open public comment period of the meeting, you must specify on your registration you wish to make a presentation. You must submit the following: (1) A written statement for each question addressed, (2) the names and addresses of all who plan to participate, (3) the approximate time requested to make your presentation. Depending on the number of presentations, FDA may have to limit the time allotted for each presentation. Presenters must submit two copies of each presentation given. If you need special accommodations due to a disability, please inform the registration contact person when you register.

## **SUPPLEMENTARY INFORMATION:**

### **I. Background**

#### *A. September 2000 Public Meeting*

On September 15, 2000, FDA held a public meeting to discuss the future of PDUFA and to listen to the views of all interested constituents. This public meeting was held as the agency began to prepare for new or amended authorizing legislation. At that meeting, the agency learned more about the expectations and concerns of various constituent groups and citizens regarding the PDUFA program. The December 7, 2001, meeting will continue this dialogue.

### *B. PDUFA I and PDUFA II*

In 1992, Congress passed PDUFA authorizing FDA to collect fees from companies that produce certain human drug and biological products. The original PDUFA (PDUFA I) had a 5-year sunset. In 1997, Congress passed the Food and Drug Administration Modernization Act (FDAMA). Part of FDAMA included an extension of PDUFA (PDUFA II) for an additional 5 years. PDUFA's original intent was to provide FDA with additional revenue so it could hire more reviewers and support staff and upgrade its information technology to speed up the application review process for human drug and biological products without compromising review quality.

### *C. Authority to Collect Fees*

The revenues are provided by a set of three fees, with one-third of the total annual revenue coming from each of the following fees: (1) Application fees for the submission of certain human drug or biological applications (in fiscal year (FY) 2001, \$309,647 per application with clinical data, and \$154,823 per application without clinical data or per supplemental application with clinical data); (2) annual establishment fees paid for each establishment that manufactures certain prescription drugs or biologicals (in FY 2001, \$145,989 per establishment); and (3) annual product fees assessed on certain prescription drug and biological products (in FY 2001, \$21,892 per product). In the aggregate, these fees are expected to generate \$135 million in FY 2002. (This is a downward adjustment-previously they had been expected to generate about \$162 million). No separate fees are charged for investigational new drug applications (INDs). However, since the review of investigational new drug applications is included in the process for the review of human drug applications, as defined in PDUFA, FDA uses some of the application, establishment, and product fees collected for the review of INDs.

### *D. Review Performance Goals*

In 1992, FDA agreed to meet a set of review performance goals that became more stringent each year, if FDA also received sufficient fee resources to enable goal achievement. These goals

applied to the review of original new human drug and biological applications, resubmissions of original applications, and supplements to approved applications. FDA met every PDUFA I performance goal.

Under PDUFA II, the review goals continue to shorten. By 2002, the PDUFA II goals call for FDA to review and act on 90 percent of the following: (1) Standard new drug and biological product applications and efficacy supplements within 10 months; (2) priority new drug and biological product applications and efficacy supplements (i.e., for products providing significant therapeutic gains) within 6 months; (3) manufacturing supplements within 6 months, and those requiring prior approval within 4 months; (4) class 1 resubmissions within 2 months, and class 2 resubmissions within 6 months.

In addition, PDUFA II added a new set of goals intended to improve FDA's responsiveness to, and communication with, industry sponsors during the early years of drug development. These goals specify timeframes for activities such as scheduling meetings and responding to various sponsor requests.

#### *E. Impact on Drug Review Process*

While PDUFA's original intent was to speed up the review process, PDUFA II's intent is to speed up the entire drug development process. By providing an influx of needed resources, PDUFA has had a dramatic and undeniable impact on the drug review process. Total resources for drug review activities have increased from \$120 million in 1992, before PDUFA was enacted, to an estimated \$329 million in FY 2002, a little more than half of which will come from fees paid by industry. These resources allowed FDA to increase its drug and biological review staff by almost 60 percent between 1993 and 1997, adding about 660 staff-years to the program by 1997. By the end of PDUFA II in 2002, FDA expects to have added another 340 staff-years of effort to this program. These additional staff, and resources to support them, have enabled FDA to respond more rapidly to new drug and biologic applications without compromising review quality.

While it is important to note that PDUFA's goals specify decision times, not approval times, both decision and approval times have decreased dramatically. Total approval time, the time from the initial submission of a marketing application to the issuance of an approval letter, has dropped from a pre-PDUFA median of 23 months to an estimated 15 months in 2001. Total approval time for priority applications, those for products providing significant therapeutic gains, has dropped from a median of over 12 months in the early PDUFA years to 6 months. In addition, because FDA has put greater effort into communicating what it expects applicants to submit, a higher percentage of applications are being approved. Before PDUFA, only about 60 percent of the applications submitted were ultimately approved. Now, about 80 percent are approved. For the consumer, this has meant more products available more quickly.

#### *F. Challenges*

Notwithstanding these successes, the agency has encountered challenges in trying to meet the PDUFA II goals. Assuring that enough appropriated funds are spent on the process for the review of human drug applications to meet requirements of PDUFA, and at the same time spending our resources in a way that best protects the health and safety of the American people, is becoming increasingly difficult. Each year, the amount that FDA must spend from appropriations on the drug review process is increased by an inflation factor. Yet, since 1992, FDA has not received increased appropriations to cover the costs of the across-the-board pay increases that must be given to all employees. The result is that our workforce and real resources for most programs other than PDUFA have contracted each year since 1992 while we struggle to ensure that enough funds are spent on the drug review process to meet this PDUFA requirement. FDA will be unable to continue to reduce staffing levels in FDA programs other than drug review and still maintain those programs in a way that best protects and promotes the public health and merits public confidence.

Another challenge we have faced in PDUFA II is that we underestimated the resources we would need to meet the new, demanding PDUFA II goals. In addition, the fees we have collected have been significantly less than expected. Revenues have been lower than projected due to the

reduced number of fee-paying applications and the increased number of fee-waived applications. This has also resulted in lower than expected fee revenues from products and establishments. In FY 2001, about 30 percent of applications received fee waivers. FDA will need to spend all of the reserve funds available in order to try to continue to meet PDUFA goals. FDA anticipates that by the end of PDUFA II the agency will have depleted all fee reserves.

Despite this fluctuation in revenues, our workload under PDUFA II continued to rise. Many of the activities covered by PDUFA II performance goals do not, themselves, generate fees, yet the workload in these areas has been substantial. For example, the numbers of commercial INDs, efficacy supplements, and manufacturing supplements are up, and the number of meetings, responses to clinical holds and special protocol assessments, all of which have specific PDUFA II performance goals, have been higher than anticipated. The new pediatric and fast track provisions of FDAMA, none of which received specific additional funding, also have contributed significantly to this increased workload.

FDA is also concerned about the safety of new drugs and biologics following approval and marketing. FDA's postmarket monitoring activities are not currently funded by PDUFA. More rigorous safety monitoring of newly approved drugs in the first few years after a product is on the market could help to detect unanticipated problems earlier. The current system for detecting adverse drug and biologics events does not provide sufficient data on the actual incidence of problems. Another concern is the growth in prescription drug advertising. Current PDUFA funding does not cover the agency's cost of reviewing promotional materials (over 37,000 pieces in 2000).

Although FDA has been able to meet most of its performance goals despite these challenges, we do not believe this will continue in the future. We do not foresee increasing or even maintaining performance levels until resources are available to meet the increased workload. These resources can be provided either from appropriated dollars or from user fees. However, to date we have not seen increases in appropriated dollars needed to meet the shortfalls we have experienced.

We may, in fact, be seeing that our efforts to meet the new PDUFA II goals have led to an unintended consequence regarding approval times of standard new drug and biologics applications. These approval times have begun to increase because more applications require multiple review cycles to reach approval. We believe this may be due to the fact that reviewers, pressed to meet the new PDUFA II goals for drug development (e.g., meetings, special protocol assessments, and responses to clinical holds), have had less time to devote to resolving last minute problems with these standard applications in time to meet the action goal date. As a result, the application must undergo an additional review cycle with its attendant timeframes and goals. Our statistics on this trend are preliminary and we are watching it closely. However, if our user fee program is to continue, it must be on a sound financial footing and based on reliable estimates of workload and resources.

## **II. Scope of Discussion**

The legislative authority for PDUFA II expires at the end of September 2002. Without further legislation the fees and resources it has provided will also expire. Public input is important at this time as final preparations are being made to propose reauthorization. Section 903(b) of the act (21 U.S.C. 393(b)) encourages FDA to consult with stakeholders, as appropriate, in carrying out agency responsibilities. Accordingly, FDA will convene a public meeting on December 7, 2001. Interested persons are invited to attend and present their views. A list of questions that we are asking interested parties to address at this meeting follows:

1. Has PDUFA supported FDA's mission to protect and promote public health? What should be retained or changed to enhance the program?
2. Should PDUFA allow the use of user fee funding to monitor safety after new drug or biologic approval?
3. How can FDA ensure that PDUFA goals are met if there continues to be a funding shortfall? If the funding shortfall persists, should FDA, in order to best protect and promote the public health,

set review priorities and, if so, how? Should there be flexibility in setting user fees to cover the increased cost of the program?

### **III. Comments**

Interested persons may submit to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, written comments on or before January 25, 2002. Submit electronic comments to [fdadockets@oc.fda.gov](mailto:fdadockets@oc.fda.gov) or <http://www.accessdata.fda.gov/scripts/oc/dockets/edockethome.cfm>. You should annotate and organize your comments to identify the specific questions to which they refer. (See above.) You must submit two copies of comments, identified with the docket number found in brackets in the heading of this document. You may review received comments approximately 15 days after the meeting in the Dockets Management Branch, Monday through Friday between 9 a.m. and 4 p.m. or on the Internet at <http://www.fda.gov/oc/pdufa/meeting2001/>.

### **IV. Transcripts**

You may request a copy of the transcript in writing from the Freedom of Information Office (HFI-35), Food and Drug Administration, 5600 Fishers Lane, rm. 12A-16, Rockville, MD 20857, approximately 15 days after the meeting at a cost of 10 cents per page. You may also examine the transcript Monday through Friday between 9 a.m. and 4 p.m. in the Dockets Management Branch or on the Internet at <http://www.fda.gov/oc/pdufa/meeting2001/>.

**V. Electronic Access**

Persons with access to the Internet may obtain more information about PDUFA at <http://www.fda.gov/oc/pdufa/default.htm>.

Dated: \_\_\_\_\_

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