



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-1895]

Prescription Drug User Fee Act; Public Meeting; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing a public meeting to discuss proposed recommendations for the reauthorization of the Prescription Drug User Fee Act (PDUFA) for fiscal years (FYs) 2018 through 2022. PDUFA authorizes FDA to collect fees and use them for the process for the review of human drug applications. The current legislative authority for PDUFA expires in September 2017. At that time, new legislation will be required for FDA to continue collecting prescription drug user fees in future fiscal years.

Following discussions with the regulated industry and periodic consultations with public stakeholders, the Federal Food, Drug, and Cosmetic Act (the FD&C Act) directs FDA to publish the recommendations for the reauthorized program 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. FDA will then consider such public views and comments and revise such recommendations as necessary.

DATES: The public meeting will be held on August 15, 2016, from 9 a.m. to 2 p.m. Please register for the meeting by August 8, 2016, at <http://pdufareauthorization.eventbrite.com>.

Submit electronic or written comments to the public docket by August 22, 2016.

ADDRESSES: The meeting and workshop will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (rm. 1503, Section A), Silver Spring, MD 20993-0002. Participants must enter through Building 1 and undergo security screening. For more information on parking and security procedures, please refer to <http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2016-N-1895 for "Prescription Drug User Fee Act; Public Meeting." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of

Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FDA will post the agenda approximately 5 days before the meeting at:

<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm>.

FOR FURTHER INFORMATION CONTACT: Graham Thompson, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 1146, Silver Spring, MD 20993, 301-796-5003, FAX: 301-847-8443, graham.thompson@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Introduction

FDA is announcing a public meeting to discuss proposed recommendations for the reauthorization of PDUFA, the legislation that authorizes FDA to collect user fees and use them for the process for the review of human drug applications. The current authorization of the

program (PDUFA V) expires in September 2017. Without new legislation, FDA will no longer be able to collect user fees for future fiscal years to fund the process for the review of human drug applications. Section 736B(d)(4) of the FD&C Act (21 U.S.C. 379h-2(d)(4)) requires that after FDA holds negotiations with regulated industry and periodic consultations with stakeholders, we do the following: (1) Present recommendations to the relevant Congressional committees, (2) publish recommendations in the Federal Register, (3) provide a period of 30 days for the public to provide written comments on the recommendations, (4) hold a meeting at which the public may present its views, and (5) after consideration of public views and comments, revise the recommendations as necessary.

This notice, the 30-day comment period, and the public meeting will satisfy some of these requirements. After the public meeting, we will revise the recommendations as necessary and present our proposed recommendations to the Congressional committees.

The purpose of the meeting is to hear the public's views on the proposed recommendations for the reauthorized program (PDUFA VI). The following information is provided to help potential meeting participants better understand the history and evolution of the PDUFA program and the current status of the proposed PDUFA VI recommendations.

II. What is PDUFA and What Does It Do?

PDUFA is a law that authorizes FDA to collect fees from drug companies that submit marketing applications for certain human drug and biological products. PDUFA was originally enacted in 1992 as the Prescription Drug User Fee Act (Pub. L. 102-571) for a period of 5 years. In 1997, Congress passed the FDA Modernization Act (FDAMA, Pub. L. 105-115) that reauthorized the program (PDUFA II) for an additional 5 years. In 2002, Congress extended PDUFA again through FY 2007 (PDUFA III) in the Public Health Security and Bioterrorism

Preparedness and Response Act (Pub. L. 107-188). In 2007, Title I of the Food and Drug Administration Amendments Act of 2007 (FDAAA, Pub. L. 110-85) reauthorized PDUFA through FY 2012 (PDUFA IV). Most recently, PDUFA was reauthorized through FY 2017 (PDUFA V) as Title I of the Food and Drug Administration Safety and Innovation Act (FDASIA, Pub. L. 112-144).

PDUFA's intent is to provide additional revenues so that FDA can hire more staff, improve systems, and establish a better-managed human drug review process to make important therapies available to patients sooner without compromising review quality or FDA's high standards for safety, efficacy, and quality. As part of FDA's agreement with industry during each reauthorization, the Agency agrees to certain performance goals. These goals apply to the process for the review of new human drug and biological product applications, resubmissions of original applications, and supplements to approved applications. During the first few years of PDUFA I, the additional funding enabled FDA to eliminate backlogs of original applications and supplements. 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 within 6 months of submission of a complete application; to review and act on 90 percent of standard original NDAs, BLAs, and efficacy supplements within 12 months; and to review and act on resubmissions and manufacturing supplements within 6 months. Over the course of PDUFA I, FDA exceeded all of these performance goals and significantly reduced median review times of both priority and standard NDAs and BLAs.

Under PDUFA II, some of the review performance goals were shortened and new procedural goals were added to improve FDA's interactions with industry sponsors and to help facilitate the drug development process. The procedural goals, for example, articulated

timeframes for scheduling sponsor-requested meetings intended to address issues or questions regarding specific drug development programs, as well as timeframes for the timely response to industry-submitted questions on special study protocols. FDA met or exceeded nearly all of the review and procedural goals under PDUFA II. However, concerns grew that overworked review teams often had to return applications as "approvable" because they did not have the resources and sufficient staff time to work with the sponsors to resolve issues so that applications could be approved in the first review cycle.

A sound financial footing and support for limited postmarket risk management were key themes of PDUFA III. Base user fee resources were significantly increased and a mechanism to account for changes in human drug review workload was adopted. PDUFA III also expanded the scope of user fee activities to include postmarket surveillance of new therapies for up to 3 years after marketing approval. FDA committed to the development of guidance for industry on risk assessment, risk management, and pharmacovigilance as well as guidance to review staff and industry on good review management principles and practices (GRMPs). Initiatives to improve application submissions and Agency-sponsored interactions during the drug development and application review processes were also adopted.

With PDUFA's reauthorization under FDAAA Title I (PDUFA IV), FDA obtained a significant increase in base fee funding and committed to full implementation of GRMPs, which includes providing a planned review timeline for premarket review, development of new guidance for industry on innovative clinical trials, modernization of postmarket safety, and elimination of the 3-year limitation on fee support for postmarket surveillance. Additional provisions in FDAAA (Titles IV, V, and IX) gave FDA additional statutory authority that increased the pre- and postmarket review process requirements, added new deadlines, and

effectively increased review workload. Specifically, the new provisions expanded FDA's drug safety authorities such as the authority to require risk evaluation mitigation strategies, order safety labeling changes, and require postmarket studies.

With the current authorization of PDUFA under Title I of FDASIA, FDA implemented a new review program ("the Program") to promote greater transparency and increase communication between the FDA review team and the applicant on the most innovative products reviewed by the Agency. The Program applies to all new molecular entity (NME) NDAs and original BLAs received by the Agency from October 1, 2012, through September 30, 2017. The Program adds new opportunities for communication between the FDA review team and the applicant during review of a marketing application, including mid-cycle communications and late-cycle meetings, while adding 60 days to the review clock to provide for this increased interaction and to address review issues for these complex applications. PDUFA V also required two assessments of the impact of the Program. The first of these, the interim assessment, is available on FDA's Web site at <http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM436448.pdf>.

In addition to continued commitment to a significant set of review, processing, and procedural goals, PDUFA V also included commitments related to enhancing regulatory science and expediting drug development, enhancing benefit-risk assessment in regulatory decisionmaking, modernizing the FDA drug safety system, and improving the efficiency of human drug application review by requiring electronic submissions and standardization of electronic drug application data. The PDUFA V Commitment Letter requires that FDA report on the progress in satisfying these commitments in the annual PDUFA performance report. The

annual performance reports can be found at

<http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm2007449.htm>. More information about FDA's implementation of PDUFA V can also be found at

<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm>.

III. Proposed PDUFA VI Recommendations

In preparing the proposed recommendations to Congress for PDUFA reauthorization, FDA conducted discussions with the regulated industry and consulted with stakeholders, as required by the law. We began the PDUFA reauthorization process by publishing a notice in the Federal Register requesting public input on the reauthorization and announcing a public meeting that was held on July 15, 2015. The meeting included presentations by FDA and a series of panels with representatives of different stakeholder groups, including patient advocates, consumer groups, regulated industry, health professionals, and academic researchers. The materials from the meeting, including a transcript and Webcast recording, can be found at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm>.

Following the July 2015 public meeting, FDA conducted negotiations with the regulated industry and held monthly consultations with stakeholders from September 2015 through February 2016. As directed by Congress, FDA posted minutes of these meetings on its Web site at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm>.

The proposed enhancements for PDUFA VI address many of the top priorities identified by public stakeholders, the regulated industry, and FDA. While some of the proposed enhancements are new, many either build on successful enhancements or refine elements from the existing program. The enhancements are proposed in the following areas: Premarket review,

regulatory decision tools, postmarketing evaluation, electronic submissions and data standards, and administrative areas (hiring and financial management). The full text of the proposed PDUFA VI commitment letter can be found here at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm>. Each significant new or modified enhancement is described briefly below:

A. Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs

The program for enhanced review transparency and communication for NME NDAs and original BLAs (the Program), first established in PDUFA V, provides for additional communication between FDA review teams and the applicants of NME NDAs or original BLAs in the form of pre-submission meetings, mid-cycle communications, and late-cycle meetings, while also adding 60 days to the review timeframe to accommodate this additional interaction. An interim assessment of the Program suggested that the Program has created conditions that enhance the ability of applicants and FDA reviewers to work toward application approval in the first cycle (see <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm327030.htm>).

For PDUFA VI, FDA proposes to maintain the Program with minor modifications to reduce administrative burden and increase flexibility to the benefit of FDA review teams and applicants. FDA proposes to provide an option for the FDA review team and the applicant to agree on a formal communication plan to govern interactions during the application review. The formal communication plan may or may not include Program elements (e.g. mid-cycle communication, late-cycle meeting) and may include other interactions that are not part of the Program (e.g. application orientation meetings). Additional flexibility is also provided for

scheduling of advisory committee (AC) meetings and an option for an informal teleconference following the AC meeting is provided as well for purposes of discussing the committee's input. Review activities involving FDA's controlled substance scheduling recommendations are also to be discussed at Program meetings, if relevant. Applications that receive a refuse-to-file action and are subsequently filed over protest are now subject to the Program review performance goals, but do not benefit from the Program interactions; additionally any subsequent resubmissions for applications filed over protest are not subject to any review performance goals.

This enhancement is described in section I.B. of the proposed PDUFA VI commitment letter.

B. Goal Extensions for Missing Manufacturing Facilities

Inspections late in the review process of inadequately identified manufacturing facilities can adversely impact FDA's ability to complete application review within the performance goal timeframes. FDA proposes to extend the goal date for an original application or an efficacy supplement when it identifies a need to inspect a facility that was not included in a comprehensive and readily located list of manufacturing facilities. This enhancement is described in section I.A.5.b of the proposed PDUFA VI commitment letter.

C. Meeting Management

The number of requests for formal meetings between sponsors and the FDA is rapidly increasing; in FY 2015 alone, FDA received over 3,000 requests for formal PDUFA meetings with sponsors. The background packages for these meetings are increasingly complex which creates challenges for FDA to review and deliberate internally before providing advice to sponsors on complex drug development questions within current performance goal timeframes. To help address this issue, FDA proposes to create a new Type B End of Phase (EOP) meeting

type for certain EOP 1 and EOP 2/pre-phase 3 meetings. The performance goal timeframes for responses to meeting requests, submission of meeting background packages, and FDA's issuance of preliminary responses for the Type B (EOP) meetings and the Type C meetings would be modified to provide adequate time for FDA review and response. Sponsors would receive preliminary responses to their questions no later than five calendar days before the scheduled meeting, providing the sponsor with time to evaluate whether an in-person meeting would still be necessary. Sponsors would also be able to request a Written Response Only for any meeting type. The language for meeting management is described in section I.H of the proposed PDUFA VI commitment letter.

D. Enhancing Regulatory Science and Expediting Drug Development

The enhancements under this section focus on enhancing regulatory science and expediting drug development. Regulatory science, in this context, is the science of developing and applying new tools, standards, and approaches to assess the safety, effectiveness, quality, and performance of FDA-regulated drug products. The details of these enhancements can be found in section I.I of the proposed PDUFA VI commitment letter.

1. FDA-Sponsor Communication During Drug Development

FDA recognizes that timely interactive communication with sponsors can help foster efficient and effective drug development. Under commitments in PDUFA V, FDA focused on improving communication between FDA and sponsors during drug development by establishing a dedicated drug development communications and training staff in the Center for Drug Evaluation and Research (CDER) and augmenting existing communications staff in the Center for Biologics Evaluation and Research (CBER). Under PDUFA VI, FDA proposes to build on this enhancement by conducting a third-party evaluation of current communication practices

between FDA and sponsors during drug development, to convene a public workshop to discuss results of this evaluation, and then to update the guidance on "Best Practices for Communication Between IND Sponsors and FDA During Drug Development," if necessary (available here: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm475586.pdf>).

2. Breakthrough Therapies

FDASIA established a new designation, breakthrough therapy, for drugs intended to treat a serious or life threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Utilization of the breakthrough therapy program has been higher than anticipated with over 300 requests for designation received, and over 100 granted (as of March 2016). Additional resources will enable the FDA to continue to work closely with sponsors throughout the development and review of breakthrough therapies. Both the FDA and the regulated industry are committed to ensuring the expedited development and review of innovative therapies for serious or life-threatening diseases by investing additional resources in the breakthrough therapy program during PDUFA VI.

3. Early Consultation on New Surrogate Endpoints

FDA recognizes that early consultation can be important to an efficient development program when a sponsor intends to use a biomarker as a new surrogate endpoint that has never been used as the primary basis for product approval in the proposed context of use. Early consultation enables the FDA review team to consult with senior management to evaluate the sponsor's proposal before providing advice to the sponsor on a critical aspect of their development program. FDA proposes that these requests for early consultation in PDUFA VI be

considered as Type C meeting requests. The purpose of the meeting will be to discuss the feasibility of the surrogate as a primary endpoint, any knowledge gaps, and how these gaps should be addressed before the surrogate endpoint could be used as the primary basis for approval. To qualify for this consultation, the meeting background package will be due at the time of the meeting request and must include preliminary human data indicating the impact of the drug on the biomarker.

4. Rare Disease Drug Development

In PDUFA VI, FDA proposes to build on the success of the Rare Disease Program (RDP) by continuing to advance and facilitate the development and timely approval of drugs and biologics for rare diseases, including diseases in children. In addition to providing training for review staff related to development and review of drugs for rare diseases and engaging in outreach to external stakeholders, the RDP staff in CDER will be integrated into review teams for rare disease development programs and application review, while the RDP Staff in CBER will ensure that CBER's review offices consider flexible and feasible approaches in review. The RDP will also continue to foster collaborations in the development of tools to support rare disease drug development and facilitate interactions between stakeholders to increase awareness of FDA regulatory programs and engagement of patients in FDA's regulatory decisionmaking.

5. Advancing Development of Drug-Device and Biologic-Device Combination Products Regulated by CBER and CDER

Under PDUFA VI FDA will pursue the opportunity to improve inter-center and intra-center combination review coordination and transparency for PDUFA-led products. FDA proposes to enhance staff capacity and capability across the relevant medical product centers and the Office of Combination Products to more efficiently, effectively, and consistently review drug

and device-led combination products. FDA also proposes to streamline the process for combination product review and to improve the Agency's ability to track drug and device-led combination product review workload, including a third party assessment of current practices for combination drug product review.

Under this enhancement FDA will also establish new performance goals and submission procedures for the review of human factors protocols for PDUFA combination products. These goals will be to provide the sponsor with written comments on these protocols within 60 days of receipt. The goals to provide written comments within 60 days will begin at the 50 percent level in FY 2019, and increase to 90 percent by FY 2021.

In addition, FDA proposes to publish draft guidance or update previously published guidance on bridging studies and patient-oriented labeling.

6. Enhancing Use of Real World Evidence for Use in Regulatory Decisionmaking

FDA recognizes the potential value of utilizing "real-world" evidence in evaluating not only the safety of medications but also their effectiveness. To better understand how real-world evidence can be generated and used appropriately in product evaluation, FDA proposes to conduct one or more public workshops, as well as other appropriate activities (e.g. pilot studies or methodology development projects). Considering the available input, FDA will then publish draft guidance on how real-world evidence can contribute to the assessment of safety and effectiveness in regulatory submissions.

7. Enhancing Regulatory Decision Tools to Support Drug Development and Review

The enhancements under this section focus on enhancing regulatory decision tools to support drug development and review. The details of these enhancements can be found in section I.J of the proposed PDUFA VI commitment letter.

8. Enhancing the Incorporation of the Patient's Voice in Drug Development and Decisionmaking

In PDUFA V, FDA conducted a series of Patient-Focused Drug Development (PFDD) meetings with the aim to more systematically gather patients' perspectives on their condition and available therapies to treat their condition. Under PDUFA VI, FDA proposes to build on these efforts to bridge from PFDD meetings to fit-for-purpose tools to collect meaningful patient input that can be incorporated into regulatory review. FDA proposes to develop a series of guidance documents to advance the collection of meaningful patient input. The publication of each draft guidance will be preceded by a public workshop conducted by FDA to gather stakeholder input relevant to the topics that will be the focus of that guidance. FDA also proposes to publish a repository of publicly available tools on FDA's Web site as a resource for stakeholders, to update internal policies and procedures, as appropriate, to incorporate an increased focus on patient input, and to enhance staff capacity to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions.

9. Enhancing Benefit-Risk Assessment in Regulatory Decisionmaking

Ensuring the safety, effectiveness, and quality of drug products is an increasingly complicated regulatory task, requiring FDA's expert consideration of a multitude of complex factors. During PDUFA V, FDA implemented an enhanced structured approach to benefit-risk assessment in regulatory decisionmaking for drug products. In PDUFA VI, FDA proposes to publish an update to its benefit-risk framework implementation plan, to conduct an evaluation of the implementation of the benefit-risk framework, to develop guidance on benefit-risk assessments for new drugs and biologics, and to revise relevant policies and procedures to include new approaches that incorporate the benefit-risk framework into the human drug review program.

10. Advancing Model-Informed Drug Development

The development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources can be used to inform regulatory decision-making, for example, in determining patient selection in clinical trials, individualized dosing for specific populations, or the need for post-marketing studies. To facilitate the development and application of these approaches during PDUFA VI, FDA proposes to convene a series of workshops to identify best practices for model-informed drug development (MIDD), to conduct a pilot program, to develop guidance on MIDD, and to update policies and procedures, as appropriate, to incorporate guidelines for the evaluation of MIDD approaches.

11. Enhancing Capacity to Review Complex Innovative Designs

To facilitate the advancement and use of complex adaptive, Bayesian, and other novel clinical trial designs during PDUFA VI, FDA proposes to convene a public workshop on complex innovative trial designs, publish guidance on complex innovative trial designs, to conduct a pilot program, and to update policies and procedures as appropriate to incorporate guidelines on evaluating complex innovative trial designs.

12. Enhancing Capacity to Support Analysis Data Standards for Product Development and Review

As regulatory submissions are increasingly submitted in fully standard electronic format, it becomes increasingly important to ensure that analysis datasets are structured according to the standards to facilitate acceptance and analysis of the datasets. To support the enhancement of analysis data standards for product development and review in PDUFA VI, FDA proposes to enhance staff capacity to develop and update relevant standards, to support the efficient submission and review of analysis datasets, to convene a public workshop to advance the

development and application of analysis data standards, to collaborate with external stakeholders on development of data standards, and to update, as appropriate, internal policies and procedures associated with the submission and utilization of standardized analysis datasets.

13. Enhancing Drug Development Tools Qualification Pathway for Biomarkers

The Biomarker Qualification Program was established to support FDA's work with external partners to develop biomarkers that aid in the drug development process. To facilitate the enhancement of the drug development tools qualification pathway for biomarkers in PDUFA VI, FDA proposes to convene a public meeting to discuss taxonomy and a framework with standards for biomarkers used in drug development, to develop guidance on biomarker taxonomy, contexts of uses, and general evidentiary standards, and to maintain a public website to communicate a list of biomarker qualification submissions in the qualification process.

E. Enhancement and Modernization of the FDA Drug Safety System

The drug safety enhancements in PDUFA VI focus on expansion of the Sentinel System and enhancements to support the review, oversight, tracking, and communication of postmarketing drug safety issues. The enhancements are described in I.K of the proposed PDUFA VI commitment letter.

1. Advancing Postmarketing Drug Safety Evaluation Through Expansion of the Sentinel System and Integration into FDA Pharmacovigilance Activities

FDA's Sentinel Initiative is a long-term program designed to build and implement a national electronic system for monitoring the safety of FDA-approved medical products. FDA recently transitioned from the Mini-Sentinel pilot to the Sentinel System, but full utilization of the Sentinel System remains a work in progress. Continued development and integration of the Sentinel System is needed to realize the system's full value to the postmarketing safety review

process. To help realize the full value of the Sentinel System during PDUFA VI, FDA proposes to continue to expand the systems' data sources and core capabilities, to systematically integrate Sentinel into postmarketing review activities, to enhance Sentinel communication practices with sponsors and the public, and to conduct an analysis of the impact of Sentinel expansion and integration for regulatory purposes.

2. Timely and Effective Evaluation and Communication of Postmarketing Safety Findings Related to New Drugs

During PDUFA VI, FDA proposes to continue to support the review, oversight, tracking, and communication of postmarketing drug safety issues. FDA proposes to make improvements to its current processes and information technology systems to enhance the management and oversight of postmarketing drug safety issues, to update policies and procedures to provide timely notification to a sponsor, to the extent practicable, when a serious safety signal is identified, and to conduct an assessment of how its data systems and processes support review, oversight, and communication of postmarketing drug safety issues.

F. Electronic Submissions and Data Standards Activities

FDA is committed to achieving the long-term goal of improving the predictability and consistency of the electronic submission process and enhancing transparency and accountability of FDA information technology related activities. During PDUFA VI, FDA proposes to publish submission documentation, metrics, submission status, and system and process changes, to hold quarterly meetings to share performance updates between FDA and the regulated industry, to hold annual public meetings to gather stakeholder input to inform the FDA information technology strategic plan, and to collaborate with standards development organizations and

stakeholders to ensure the long-term sustainability of supported data standards. These enhancements are described in section IV of the proposed PDUFA VI commitment letter.

G. Improving FDA Hiring and Retention of Review Staff

To speed and improve development of safe and effective new therapies for patients requires that FDA hire and retain sufficient numbers and types of technical and scientific experts to efficiently conduct reviews of human drug applications. In order to strengthen this core function during PDUFA VI, FDA proposes to commit to completing implementation of an full time equivalent staff (FTE)-based position management system capability, to complete implementation of an online position classification system, to complete implementation of corporate recruiting practices, to augment hiring capacity with expert contractor support, to complete establishment of a dedicated function to ensure needed scientific staffing for the human drug review program, to establish clear goals for human drug review program hiring, and to conduct a comprehensive and continuous assessment of hiring and retention performance. These enhancements are described in section III of the proposed PDUFA VI commitment letter.

H. Enhancing Management of User Fee Resources

FDA is committed to enhancing management of PDUFA resources and ensuring PDUFA user fee resources are administered, allocated, and reported in an efficient and transparent manner. In PDUFA VI, FDA proposes to establish a resource capacity planning function to improve its ability to analyze current resource needs and project future resource needs, to modernize its time reporting approach, to conduct an evaluation of PDUFA program resource management, to publish a 5-year PDUFA financial plan with annual updates, and to convene an annual public meeting, beginning in FY 2019, to discuss the financial plan and progress towards

the financial management enhancements. These enhancements are described in section II of the proposed PDUFA VI commitment letter.

I. Enhancements to Fee Structure and Related Mechanisms for Increased Predictability, Stability, and Efficiency

The current overall PDUFA fee structure and the fee setting process were established in 1993 for PDUFA I and have generally remained in place through four reauthorizations of PDUFA. Over the years, FDA and industry agreed that some elements of the fee structure and the fee setting process could be updated to enhance the predictability and stability of fee amounts and revenues in a manner to improve FDA's ability to engage in long-term financial planning. Additionally, some elements of the fee structure reduce the efficiency of administrative work without a corresponding benefit to the public or to the regulated industry. To address these issues, FDA proposes to shift a greater proportion of the target revenue allocation to more predictable fee-paying types (20 percent to applications; 80 percent to Program fees), to discontinue the establishment and supplement fees, to rename the product fee as the PDUFA Program fee, to modify the Program fee billing date to minimize the need for multiple billing cycles, to add a limitation that a sponsor shall not be assessed more than five PDUFA Program fees for a fiscal year for products identified in each distinct approved human drug application held by that sponsor, and to discontinue the Fees-Exceed-the-Costs waiver. FDA also proposes during PDUFA VI to replace the workload adjuster with a robust methodology for adjusting fees based on the capacity needs of the program, and to replace the fifth year offset provision and final year adjustment provisions with an annual operating reserve adjustment to provide for adequate carryover resources.

J. Impact of PDUFA VI Enhancements on User Fee Revenue

To implement the proposed enhancements for PDUFA VI, funding for a cumulative total of 230 FTE staff is proposed to be phased in over the course of PDUFA VI. The new funding will be phased in as follows:

- \$20,077,793 for FY 2018
- \$21,317,472 for FY 2019
- \$16,953,329 for FY 2020
- \$5,426,896 for FY 2021
- \$2,769,609 for FY 2022

In addition, \$8.73 million will be added in FY 2018 to provide for other additional direct costs associated with the PDUFA VI enhancements. This amount will be included for FYs 2019 through 2022 after being adjusted for inflation.

IV. Purpose and Scope of the Meeting

If you wish to attend this meeting, visit <http://pdufareauthorization.eventbrite.com>. Please register by August 8, 2016. If you are unable to attend the meeting in person, you can register to view a live Webcast of the meeting. You will be asked to indicate in your registration if you plan to attend in person or via the Webcast. Seating will be limited, so early registration is recommended. Registration is free and will be on a first-come, first-served basis. However, FDA may limit the number of participants from each organization based on space limitations. Registrants will receive confirmation once they have been accepted. Onsite registration on the day of the meeting will be based on space availability. If you need special accommodations because of a disability, please contact Graham Thompson (see FOR FURTHER INFORMATION CONTACT) at least 7 days before the meeting.

The meeting will include a presentation by FDA and a series of invited panels representing different stakeholder groups identified in the statute (such as patient advocacy groups, consumer advocacy groups, health professionals, and regulated industry). We will also provide an opportunity for other organizations and individuals to make presentations at the meeting or to submit written comments to the docket before the meeting.

FDA will also hold an open public comment period at the meeting to give the public an opportunity to present their comments. Registration for open public comment will occur at the registration desk on the day of the meeting and workshop on a first-come, first-served basis.

Transcripts: As soon as a transcript is available, FDA will post it at <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm446608.htm>.

Dated: July 13, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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