PDUFA
Background and Reauthorization Process

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Outline for this briefing

- PDUFA Background
- Financial Background and Fee Structure
- Workload and Performance
- PDUFA VI Commitments & Accomplishments
- Reauthorization Process Overview

Before 1992, timeliness of FDA drug review was a big concern

PDUFA I

- User fees added resources for more review staff to eliminate the backlog of overdue applications and improve review timeliness
- FDA agreed to meet specific performance goals

Result:

- More predictable, streamlined process
- Patients gained earlier access to new drugs and biologics approved since 1992
- Overall, clinical development time and average time to approval dropped since 1992
- However, a recent Tufts study looking at the past decade, notes that while FDA review times for approvals continue to drop, development time has increased for certain non-orphan drugs*

** Source: Tufts Center for the Study of Drug Development, Impact Report Vol. 22 No. 4, July/Aug. 2020*

Basic PDUFA construct

- Fee funds are added to appropriated funds and are intended to increase staffing and other resources to speed and enhance review process
- User fees pay for services that directly benefit fee payers*
- Fee discussions with industry focus on desired enhancements in terms of specific aspects of activities in “process for the review of human drugs”
  - What new or enhanced process will the FDA want or industry seek to include in the next 5 years?
  - What is technically feasible?
  - What resources are required to implement and sustain these enhancements?
  - No discussion of policy.
- Experience: *Devil is in the Details*

** OMB Circular A-25; direct benefit distinguishes user fees from tax*

Performance commitments and fee funding have evolved since 1992

PDUFA | *1993-1997*
Added funds for pre-market review; reduced backlog and set predictable timelines (goals) for review action

PDUFA II (FDAMA) | *1998-2002*
Shortened review timelines, added review goals; added process and procedure goals; added some funding

PDUFA III (BT Preparedness & Response Act) | *2003-2007*
Significantly added funding; increased interaction in first review cycle (GRMPs); allowed limited support for post-market safety

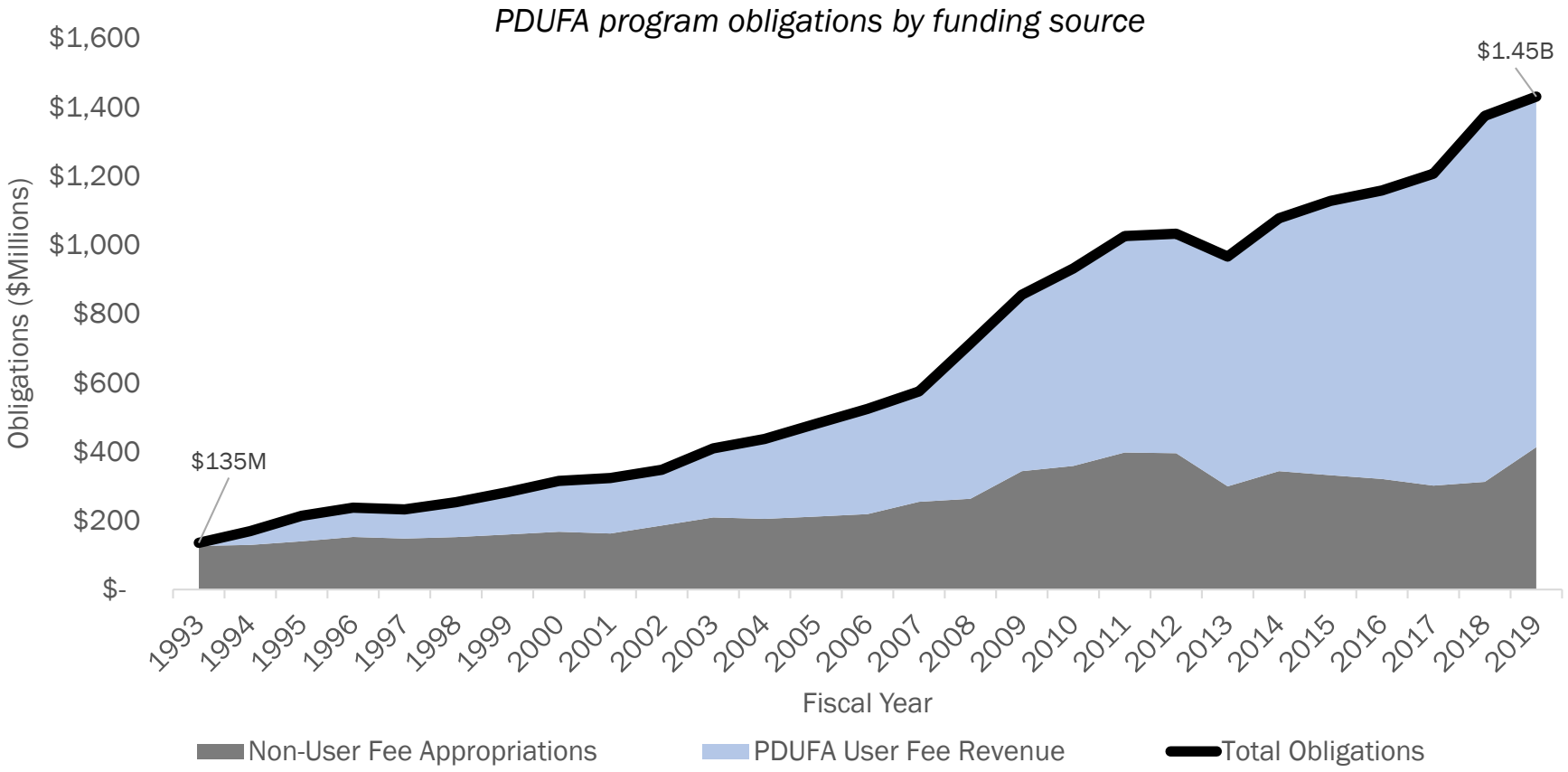
PDUFA IV (FDAAA) | *2008-2012*
Increased and stabilized base funding; enhanced pre-market review; modernized post-market safety system

PDUFA V (FDASIA) | *2013-2017*
Small increase to base funding; review enhancements increased communication with sponsors; strengthened regulatory science & post-market safety; set electronic data standards

PDUFA VI (FDARA) | *2018-2022*
Modernized the user fee structure; focused on HR and financial management improvement; created capacity planning capability; enhanced use of regulatory tools via benefit-risk, patient-focused drug development, complex innovative trial designs, model informed drug development; enhanced staffing for breakthrough therapy reviews; focused on communication with industry; explored RWE in regulatory decision-making

User fee revenue is critical to the program

User fee revenue has outpaced budget authority available for the program



PDUFA user fee revenue funded **7%** of the program in FY1993 to **71%** in FY2019.

Current Fee Structure

- PDUFA VI modernized the user fee structure to improve program funding predictability, stability, and administrative efficiency.
- The new structure eliminated the supplement fees, replaced the establishment and product fees with a program fee, and shifted a greater proportion of the target revenue to the new more predictable and stable annual program fee.
- FY 2020 target revenue is $1,074,714,000.
  - 20% collected from applications ($214,942,800 collected from ~73 fee paying full application equivalents)
  - 80% collected from the PDUFA programs ($859,771,200 collected from 2,642 program fees)

Fee Type	FY2020 Fee Amount
Applications with clinical data	$2,942,965
Applications without clinical data	$1,471,483
PDUFA program fee	$325,424

Workload & Performance

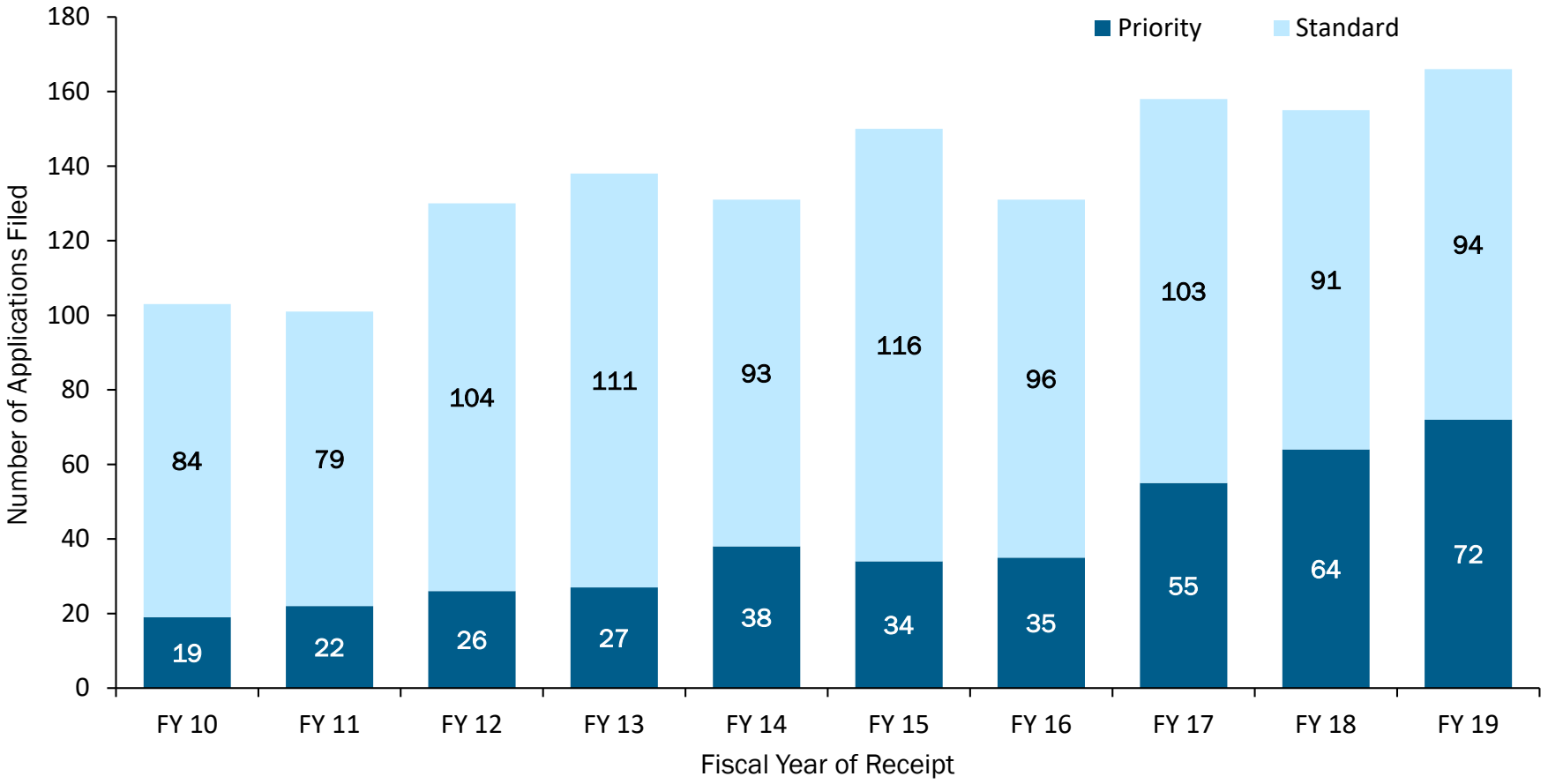
Fees support review work against a broad set of performance commitments

31 specific review & procedural goals most with specific and aggressive timeframes; in addition to other commitments

EXAMPLE	GOAL
NMEs & Original BLAs	90% of priority applications within 8 months *(6 months of filing date)* 90% of standard applications within 12 months *(10 months of filing date)*
Original non-NME NDAs and Original Efficacy Supplements	90% of priority applications within 6 months 90% of standard applications within 10 months
NDA/BLA Efficacy Supplement Resubmissions	90% of Class 1 resubmissions within 2 months 90% of Class 2 resubmissions within 6 months
Manufacturing Supplements	90% of prior approval supplements within 4 months 90% of non-prior approval supplements within 6 months
Special Protocol Assessments (SPA)	90% of SPAs within 45 days of receipt
Clinical Hold Response	90% of clinical hold responses within 30 days of receipt
Meeting Scheduling	90% of Type A/B/C meetings within 30/60/75 days of receiving request

NDA and BLA workload continues to trend upwards in PDUFA VI

Total NDAs and BLAs filed



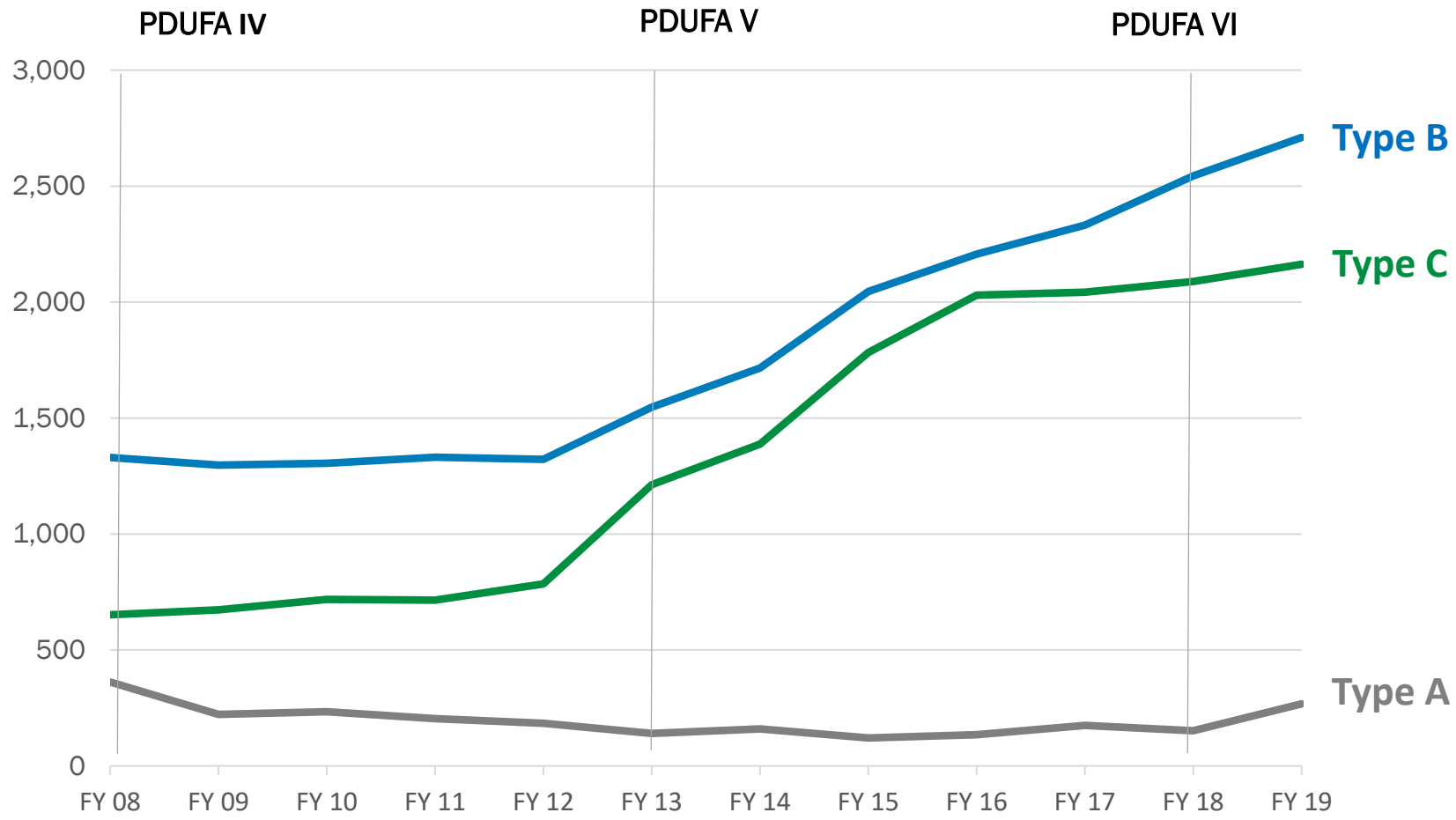
FDA meets or exceeds nearly all review goals

Submission Type	Goal: Act on 90 Percent Within	Progress*	FY 2019 Current Performance	Highest Possible Final Performance
Original Priority NMEs and BLAs	6 months of filing date	16 of 43 complete	100%	100%
Original Standard NMEs and BLAs	10 months of filing date	0 of 31 complete	–	100%
Original Priority non-NME NDAs	6 months	10 of 16 complete	100%	100%
Original Standard non-NME NDAs	10 months	11 of 63 complete	91%	98%
Class 1 Resubmitted NDAs and BLAs	2 months	5 of 7 complete	80%	86%
Class 2 Resubmitted NDAs and BLAs	6 months	19 of 41 complete	95%	98%
Priority NDA and BLA Efficacy Supplements	6 months	54 of 74 complete	98%	99%
Standard NDA and BLA Efficacy Supplements	10 months	42 of 177 complete	95%	99%
Class 1 Resubmitted NDA and BLA Efficacy Supplements	2 months	4 of 4 complete	100%	100%
Class 2 Resubmitted NDA and BLA Efficacy Supplements	6 months	1 of 2 complete	100%	100%
NDA and BLA Manufacturing Supplements requiring prior approval	4 months	671 of 993 complete	98%	99%
NDA and BLA Manufacturing Supplements not requiring prior approval	6 months	821 of 1,440 complete	99%	99%

* This column does not include undesignated applications in the total. Undesignated applications have only pending status.

PDUFA meeting workload is increasing

CDER and CBER meeting requests and written response only (WRO) workload by fiscal year (FY)



Data as of 9/30/2019
Type B EOP meetings are combined with Type B metric
Type (A)(B)(C) WRO meetings are combined with their respective meeting type metric
*2019 data is preliminary

Meeting management is a challenge

CDER and CBER meeting management performance by FY

	Performance by Fiscal Year											
Meeting Management Goal	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019**
Type A Meeting Requests	63%	74%	65%	79%	85%	91%	90%	96%	90%	91%	93%	76%
Type B Meeting Requests	83%	80%	76%	85%	85%	89%	91%	91%	92%	92%	90%	91%
Type B(EOP) Meeting Requests	–	–	–	–	–	–	–	–	–	–	80%	82%
Type C Meeting Requests	81%	78%	76%	82%	87%	87%	88%	86%	92%	92%	92%	89%
Type A Meetings Scheduled	58%	64%	66%	84%	94%	92%	73%	64%	75%	75%	75%	70%
Type B Meetings Scheduled	77%	69%	73%	90%	93%	91%	71%	72%	69%	69%	63%	63%
Type B(EOP) Meetings Scheduled	–	–	–	–	–	–	–	–	–	–	74%	76%
Type C Meetings Scheduled	79%	74%	78%	88%	91%	92%	80%	80%	77%	77%	75%	74%
Type A Written Response	–	–	–	–	–	–	–	–	–	–	67%	80%
Type B Written Response	–	–	–	–	–	71%	79%	76%	77%	77%	77%	82%
Type B(EOP) Written Response	–	–	–	–	–	–	–	–	–	–	57%	70%
Type C Written Response	–	–	–	–	–	78%	86%	81%	85%	85%	84%	80%
Preliminary response for Type B(EOP) Meetings	–	–	–	–	–	–	–	–	–	–	85%	86%
Meeting Minutes	61%	69%	68%	83%	85%	87%	90%	89%	93%	93%	91%	92%

* This column is current performance as of 9/30/19 and does not include pending FY 2019 submissions/actions at that time.

Additional PDUFA VI Accomplishments & Commitments

Behind the scenes: A growing number of enhancements and activities

In addition to the performance review goals under PDUFA VI, FDA is implementing over **200 actions to fulfill PDUFA VI performance enhancement commitments.** These include:

70+ new or updated pilots, programs or processes

60+ data/list postings to the public website

40+ public meetings or public workshops

20+ new or revised guidances

10+ public reports

Recapping additional PDUFA VI commitments and enhancements

- Regulatory Science and Expediting Drug Development
- Regulatory Decision Tools to Support Drug Development and Review
- Modernization of the FDA Drug Safety System
- Management of User Fee Resources
- Improving FDA Hiring and Retention of Review Staff
- Improving the Electronic Submission Process and Transparency of IT activities

Regulatory Science and Expediting Drug Development

Enhanced Communication in IND Phase

To continue facilitating the conduct of efficient and effective drug development programs, FDA contracted with an independent third-party to assess the current communication practices in the IND phase and recommend best practices.

Rare Diseases

The Rare Diseases Program staff is becoming more integrated into review teams by attending product-specific meetings, holding annual trainings, and participating in conferences and/or trainings with patient stakeholders.

Combination Product Review

FDA implemented a Staff Manual Guide (SMG 4101), published/revised several documents of policies and procedures, and published several draft guidances.

Real World Evidence (RWE)

To further enhance the use of RWE in regulatory decision-making, FDA co-led a public workshops on the topic and continues to oversee additional projects and activities aimed at addressing concerns and considerations in the use of RWE in regulatory decision-making.

Regulatory Decision Tools to Support Drug Development and Review

Patient Focused Drug Development

FDA has held several public meetings and published a series of guidances to further enhance the incorporation of patients' voice into drug development and decision-making.

Enhancing Benefit Risk Assessment

FDA published an update to the "Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making" implementation plan and held a meeting to gather stakeholder input on key benefit-risk topics.

Model-Informed Drug Development (MIDD)

To facilitate the development of models derived from preclinical and clinical data sources, FDA has established the MIDD pilot program, holding workshops and having published a guidance on Population Pharmacokinetics, among other activities.

Complex Innovative Designs (CID)

To facilitate the further use of complex adaptive, Bayesian, and other novel clinical trial designs, FDA established the CID program which grants meetings and increased interaction to sponsors to discuss their approach toward complex innovative trial designs.

Drug Development Tools (DDTs) Qualification Pathway

To facilitate the enhancement of the drug development tools qualification pathway for biomarkers, FDA continues to hire staff, host public meetings, and regularly post information about DDT submissions.

Modernization of the FDA Drug Safety System

Expanding Sentinel System and Integration into Pharmacovigilance Activities

FDA added capabilities to Sentinel's querying tools, held a public workshop on Implementation of Signal Detection Capabilities, and published a revised guidance on *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)3*.

Communication of Postmarketing Safety Findings

FDA updated policies and procedures concerning tracking postmarketing safety signals to include consistent and timely notifications to sponsors.

Management of User Fee Resources

Resource Capacity Planning Capability

FDA created and staffed a resource capacity planning capability to better predict future workload and understand associated resource demands. In addition, FDA developed a new capacity planning methodology that accounts for sustained increases in workload to replace the PDUFA workload adjuster.

Modernized Time Reporting

FDA is modernizing it's time reporting practices and systems in all Centers engaged in PDUFA work. CDER and CBER modernized their time reporting throughout FY 2018 and FY 2019 and FDA plans to continue modernization in CDRH, ORA, and Office of the Commissioner in subsequent years.

Financial Transparency and Efficiency

FDA contracted with an independent third party to evaluate PDUFA program resource management during FY 2018 to ensure user fee resources are administered, allocated, and reported in an efficient and transparent manner. Published PDUFA 5-year financial plans each year and held annual public meetings starting in FY 2019 to discuss the plans, along with implementation of other management of user fee resources commitments.

Improving FDA Hiring and Retention of Review Staff

Modernizing Hiring System Infrastructure

To modernize hiring system infrastructure and augment our system capacity, FDA deployed a position description library and is expecting to deploy a position-based management system.

Augmentation of Hiring Staff Capacity and Capability

Three contracts were awarded to vendors to provide continuous support for FDA's human resources capacity.

Establishment of a Dedicated Scientific Staffing Unit

FDA staffed a new HR unit focused on developing and implementing scientific staffing hiring strategies and plans.

Comprehensive and Continuous Assessment of Hiring and Retention

FDA brought on third-party contractors to conduct an initial and interim assessment of to better understand thus improve hiring practices.

Improving the Electronic Submission Process and Transparency of IT activities

Predictability and Consistency of PDUFA E-submissions

FDA has been publishing targets for Electronic Submissions Gateway (ESG) availability, current ESG operational status on the public website, and has invited industry to participate in user acceptance testing.

Transparency and Accountability of E-submissions and Data Standards Activities

Among other activities, FDA holds quarterly meetings with industry on electronic submissions and data standards and also posts regular updates to the FDA data standards catalog and to the Data Standards Action Plan.

Performance data and completed deliverables are available to the public

Completed PDUFA VI deliverables can be found on FDA's website:

https://www.fda.gov/industry/prescription-drug-user-fee-amendments/completed-pdufa-vi-deliverables

FDA released a new PDUFA performance dashboard that allows users to view and download current and historical performance data:

https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-pdufa-performance

PDUFA Reauthorization Process

PDUFA reauthorization involves significant consultation

PDUFA REAUTHORIZATION and REPORTING REQUIREMENTS.

(d) REAUTHORIZATION.—

(1) CONSULTATION.—In developing recommendations to present to the Congress with respect to the goals, and plans for meeting the goals, for the process for the review of human drug applications for the first 5 fiscal years after fiscal year 2017 and for the reauthorization of this part for such fiscal years, the Secretary shall consult with— (A) the Committee on Energy and Commerce of the House of Representatives; (B) the Committee on Health, Education, Labor, and Pensions of the Senate; (C) scientific and academic experts; (D) health care professionals; (E) representatives of patient and consumer advocacy groups; and (F) the regulated industry.

(2) PRIOR PUBLIC INPUT.—Prior to beginning negotiations with the regulated industry on the reauthorization of this part, the Secretary shall—

(A) publish a notice in the Federal Register requesting public input on the reauthorization; (B) hold a public meeting at which the public may present its views on the reauthorization, including specific suggestions for changes to the goals referred to in subsection (a); (C) provide a period of 30 days after the public meeting to obtain written comments from the public suggesting changes to this part; and (D) publish the comments on the Food and Drug Administration's Internet Web site.

(3) PERIODIC CONSULTATION.—Not less frequently than once every month during negotiations with the regulated industry, the Secretary shall hold discussions with representatives of patient and consumer advocacy groups to continue discussions of their views on the reauthorization and their suggestions for changes to this part as expressed under paragraph (2).

(4) PUBLIC REVIEW OF RECOMMENDATIONS.—After negotiations with the regulated industry, the Secretary shall— (A) present the recommendations developed under paragraph (1) to the Congressional committees specified in such paragraph; (B) publish such recommendations in the Federal Register; (C) provide for a period of 30 days for the public to provide written comments on such recommendations; (D) hold a meeting at which the public may present its views on such recommendations; and (E) after consideration of such public views and comments, revise such recommendations as necessary.

(5) TRANSMITTAL OF RECOMMENDATIONS.—Not later than January 15, 2022, the Secretary shall transmit to the Congress the revised recommendations under paragraph (4), a summary of the views and comments received under such paragraph, and any changes made to the recommendations in response to such views and comments.

(6) MINUTES OF NEGOTIATION MEETINGS.—

(A) PUBLIC AVAILABILITY.—Before presenting the recommendations developed under paragraphs (1) through (5) to the Congress, the Secretary shall make publicly available, on the public Web site of the Food and Drug Administration, minutes of all negotiation meetings conducted under this subsection between the Food and Drug Administration and the regulated industry.

(B) CONTENT.—The minutes described under subparagraph (A) shall summarize any substantive proposal made by any party to the negotiations as well as significant controversies or differences of opinion during the negotiations and their resolution.

PDUFA reauthorization involves significant consultation

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Today's Public meeting

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Federal Register Notice published for upcoming public stakeholder meetings.

Priorities for PDUFA VII

- Promote sustainable innovation in drug development
- Enhance regulatory predictability and post-market safety
- Advance the regulatory infrastructure for digital technologies and new sources of data
- Enhance operational capabilities, efficiency, and agility

THANK YOU