Biocom California
PDUFA VII

The Prescription Drug User Fee Act (PDUFA) was created to eliminate the backlog of drug applications in the early 1990s by giving the Food and Drug Administration (FDA) the authority to collect fees from industry and use them to support the review of applications. In exchange, FDA committed to meeting performance goals negotiated with industry. As a result, review times decreased from two years to ten months. PDUFA is reauthorized every five years and adds new features to modernize regulatory science and keep pace with innovation.

The PDUFA VII user fee base revenue amount for FY 2023 is $1.15 billion. Fees for FY 2023 are as follows: an application requiring covered clinical data ($3,242,026), an application not requiring covered clinical data ($1,621,013), and the prescription drug program fee ($393,933).

Legislative History:

1992: PDUFA authorized FDA to collect a fee to review products in exchange for more timely review.

1997: PDUFA II passed as Title I of the FDA Modernization Act. It enacted stricter performance goals, increased transparency, and provided better communication.

2002: PDUFA III was part of the Public Health and Bioterrorism Preparedness Act. It extended the range of activities to include pre-clinical development.

2007: PDUFA IV was signed into law with the FDA Amendments Act. It removed the 3- year limitation on post-approval activities.

2012: PDUFA V, Title I of the Food and Drug Administration Safety and Innovation Act; it included important tools such as benefit/risk analysis and patient-reported outcomes.

2017: PDUFA VI was signed into law through the FDA Reauthorization Act. It included patient-focused drug development and real-world evidence goals.

2022: PDUFA VII was signed into law as part of the Continuing Appropriations and Ukraine Supplemental Appropriations Act. This bill reauthorized the program for 5 years until 2027.

Accomplishments:

1,800
drugs and biologics approved

80%
of priority review medicines approved on the first cycle

500 treatments
for Rare Diseases.

10
months review time for standard applications

7.8
months review time for priority applications

Highlights of PDUFA VII:

Rare Disease Endpoint Advancement Pilot Program

The Rare Disease Endpoint Advancement (RDEA) Pilot program provides a mechanism for sponsors to collaborate with FDA throughout the efficacy endpoint development process. FDA will commit to holding up to 4 additional meetings with sponsors related to endpoint development and selecting programs that have applicability to other rare diseases. FDA will hold public meetings to share the lessons learned from this pilot.

Type D Meetings

This new meeting type will cover a question that raises a new issue after a formal meeting, a narrow issue on which the sponsor is seeking FDA's input with only a few associated questions, or a general question about an innovative development approach that does not require extensive advice. This meeting type is not intended to cover more than 2 topics and require input from more than 3 disciplines.

INTERACT Meetings

INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs (INTERACT) meetings are intended to facilitate Investigational New Drug (IND)-enabling efforts where the sponsor is facing a novel, challenging issue. The issues typically relate to IND requirements, such as design of IND-enabling toxicity studies, complex manufacturing technologies or processes, development of innovative devices used with a drug or biologic, or use of cutting-edge testing methodologies.

Split Real Time Application Review Pilot Program

The Split Real Time Application Review (STAR) Pilot Program seeks to shorten the time from the date of complete submission to the action date for efficacy supplements to allow earlier patient access to novel uses of existing therapies that address an unmet medical need. The applications will be split into two parts and submitted around 2 months apart. FDA intends to complete review along an expedited approval timeline and complete review at least 1 month before the PDUFA goal date.

Post-marketing Requirement Communication

PDUFA VII formalizes a timeframe for FDA communication to a sponsor about the need for any post-marketing requirements (PMRs) earlier in the review cycle in order to allow sponsors to have ample time to design and initiate the study. For standard new molecular entity (NME), new drug applications (NDA), and original biological license applications (BLA), FDA will communicate details on anticipated PMRs no later than 8 weeks prior to the PDUFA action goal date. For priority NME NDAs and original BLAs, the FDA will communicate details on anticipated PMRs to the sponsor no later than 6 weeks before the PDUFA goal date. FDA has also established a system to allow sponsors to request a review of an existing PMR for consideration of its release.

Center for Biologics Evaluation and Research

To address the dramatic increase in cell and gene therapies, PDUFA VII includes significant commitments to increasing resources for the Center for Biologics Evaluation and Research (CBER). This includes hiring 228 more staff, a full evaluation of the Center's processes, and providing extensive training for reviewers and staff. CBER will also undertake activities to increase patient-focused drug development, facilitate novel approaches to the development of cell and gene therapies, update guidance on Regenerative Medicines, and leverage knowledge from external stakeholders to improve the program.

Biocom California

Highlights of PDUFA VII:

Technology Modernization

PDUFA VII includes commitments to modernize FDA's technological abilities in order to support ever-growing data sets associated with applications, including developing a modernization strategy, supporting cloud-based submissions, and promoting bioinformatics support to handle the increase of Next Generation Sequencing data included in submissions.

Chemistry, Manufacturing and Controls Development and Readiness Pilot program

FDA will update its internal processes and establish a pilot program for Chemistry, Manufacturing, and Controls (CMC) for CBER- and CDER-regulated products that treat an unmet need and have accelerated clinical development timelines. The pilot will kick off in FY 2023 to facilitate CMC readiness and increase interaction with FDA. FDA will select between 8–10 proposals per fiscal year over a 4-year period with a public meeting to share lessons learned at the end of the pilot program term and hold two additional CMC-focused Type B meetings and CMC-focused discussions with participants.

Advancing Real-World Evidence Pilot Program

The Advancing Real-World Evidence (RWE) Pilot Program seeks to improve the quality of RWE-based approaches to support new intended labeling claims (e.g., new indications, populations, and dosing information) or satisfy post-approval study requirements. It will also develop processes that promote consistent decision-making, shared learning, and characteristics of RWE that can support regulatory decisions by allowing FDA to discuss study designs in a public forum. The pilot will accept a maximum of 16 products over the next 5-year cycle and will culminate in a public engagement on lessons learned.

Patient-Focused Drug Development

PDUFA VII furthers patient-focused drug development (PFDD) by expanding internal staff training and external outreach to sponsors and stakeholders, with an emphasis on PFDD methods and tools-related guidance and practice to achieve broad integration into regulatory decision-making across review divisions and industry development programs. FDA will also engage external experts to support the review of patient experience data, hold public meetings, and develop a catalog of standard core Clinical Outcome Assessments (COAs).

Clinical Trial Design

FDA will enhance the capacity to review complex innovative designs (CID), Bayesian and other novel clinical trial designs, and model-informed drug development (MIDD). FDA will increase public comment opportunities. They will also offer additional meetings as part of the MIDD paired program, including up to 8 programs per year, and publish a Request for Information on improving MIDD.

FDA Staffing: New Hires

FDA has committed to hiring personnel at the rate outlined below.

Fiscal Year:	CDER	CBER
2023	77	132
2024	31	48
2025	15	29
2026	0	15
2027	0	4
Total:	123	228

Timeline Highlights:

Starting October 1, 2022

- The STAR program is available to sponsors.
- CDER and CBER conduct a CMC Development and Readiness Pilot (CDRP) to facilitate the expedited CMC development of products under an IND application.
- Technology Modernization initiatives begin.
- FDA establishes an Advancing RWE Pilot Program that will accept one to two proposals each cycle until FY 2025.

Starting July 1, 2023

- Sponsors may submit proposals to the RDEA Program beginning in Q4, and FDA will accept a maximum of 1 proposal until September 30, 2023.

Starting October 1, 2023

- FDA accepts one proposal per quarter to the RDEA Program with a maximum of 3 proposals per year.
- FDA publishes additional draft guidance documents for digital health technologies.

Starting October 1, 2024

- The Advancing RWE Pilot Program accepts one to four proposals each cycle.

By September 30, 2027

FDA will have conducted or convened:

Technology Modernization:

- A multi-year modernization roadmap for CBER and IT modernization activities.
- At least 3 demonstration projects to explore the application of cloud-based technologies to improve sponsor-regulator interactions and these project outcomes will be shared with industry.

Digital Health Technologies:

A Digital Health Technology (DHT) framework to inform regulatory decision-making for drugs and biological products supported by DHT-derived data and cloud technology to handle large volumes of data from trials conducted using DHTs.

Meetings:

- 90% of Type D meetings, or send written response, within 50 calendar days from receipt of meeting request.
- 90% of INTERACT meetings, or send written response, within 75 calendar days from receipt of meeting request.

Advancing RWE:

- A public workshop/meeting to discuss RWE case studies with a focus on approaches for generating RWE for regulatory requirements.

PFDD:

A public PFDD meeting with key stakeholders to understand patient perspectives on gene therapy products and issue a meeting summary report.

Innovative Clinical Trial Methodology:

A public workshop to discuss aspects of complex adaptive, Bayesian, and other novel clinical trial designs.

STAR Pilot:

A public workshop and a report by the end of Q2 in FY 2026 to discuss the potential value and feasibility of expanding the pilot program to select NME NDAs and BLAs.

SOURCES:
https://www.fda.gov/media/151712/download
https://www.federalregister.gov/documents/2022/10/07/2022-21968/prescription-drug-user-fee-rates-for-fiscal-year-2023