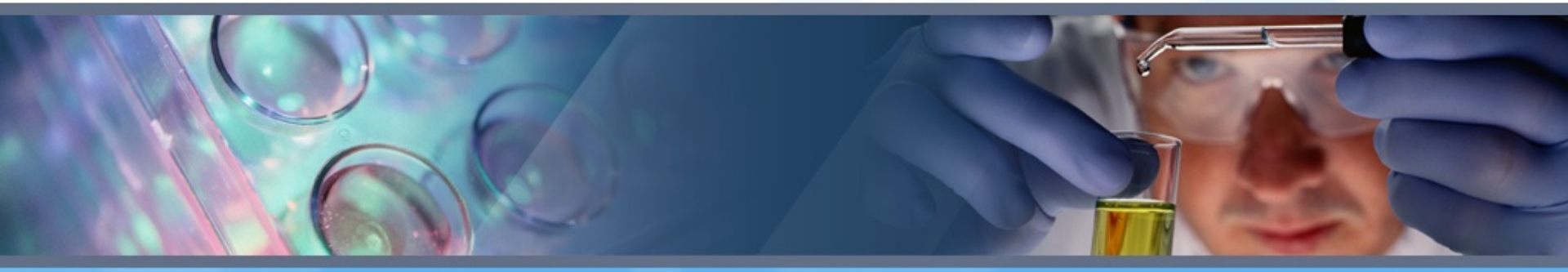
PhRMA
New Medicines. New Hope.

Bio
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

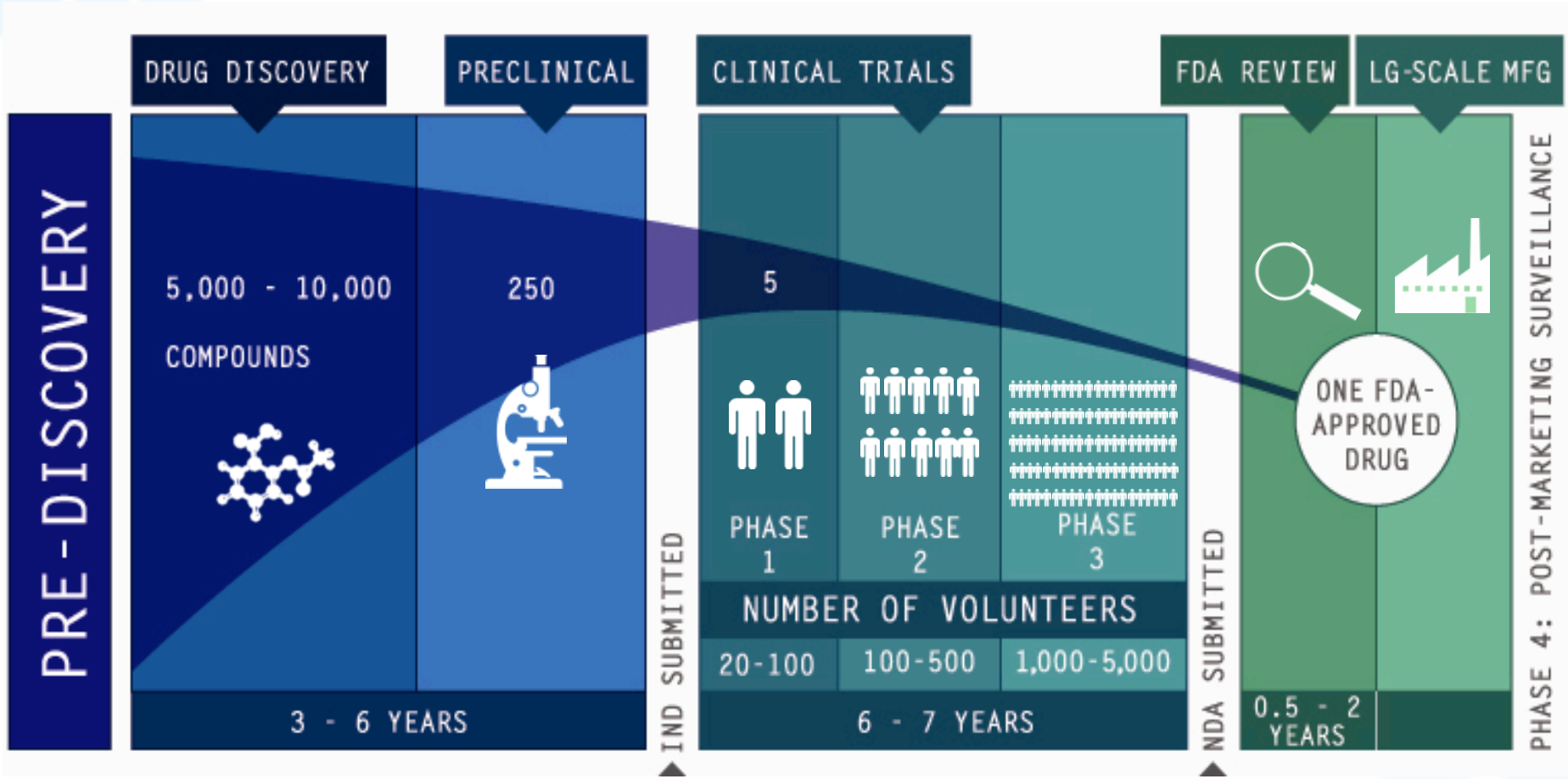


PDUFA-V Reauthorization

Highlights of Performance Goals Letter

May 2012

Drug Discovery & Development Overview: A Difficult Road



Source: Drug Discovery and Development: Understanding the R&D Process. www.innovation.org

The emerging AIDS epidemic in the 1980's sparked demand for faster review times

Protestors in New York City hold signs reading, "Safe Drugs Now"[1]

AIDS protesters demanded shorter review times

- AIDS activist group ACT UP! closed down the FDA to protest the slow process of drug approval
- ACT UP! argued that because there were few treatments for AIDS, new drugs should be reviewed as quickly as possible
- Their efforts helped lead the FDA, Congress and industry to work together to shorten drug review times

Patient protests prompted the creation of PDUFA

1. http://apps.nlm.nih.gov/ againsttheodds/exhibit/action_on_aids/fighting_discrimination.cfm

Solution to slow review times was the 1992 Prescription Drug User Fee Act (PDUFA I)

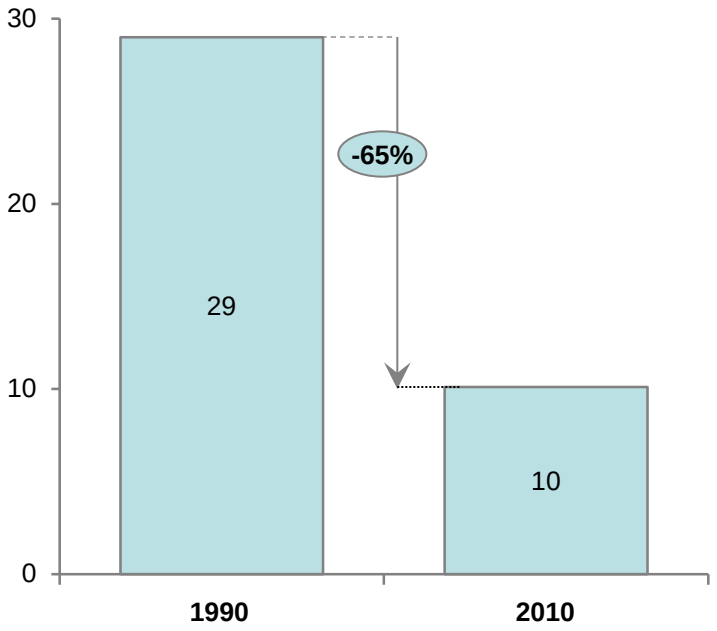
- **PDUFA Objective : Hire additional FDA drug reviewers to improve drug and biologics review times**
- **PDUFA I authorized the FDA to collect user fees from the pharmaceutical industry**
  - User fees supplement, but do not replace, Congressional appropriations
  - Fees must be reasonable
  - Revenues must be entirely dedicated to improvement of review process
- **To ensure timely reviews, FDA is required to meet certain performance benchmarks**
  - **Priority Review: 6 month goal**
    - Designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists
  - **Standard Review: 10 month goal***
    - Applied to medicines that provide therapeutic options and advance medical science

***Under PDUFA I, standard review goal was set at 12 months. This was revised to 10 months under PDUFA II**

PDUFA has significantly improved drug approval timelines

Drug review times were twice as long as today

Review time in months 1990 vs. 2010



US lagged other countries in approving new drugs

70% Percentage of new medicines first marketed overseas in late 80's

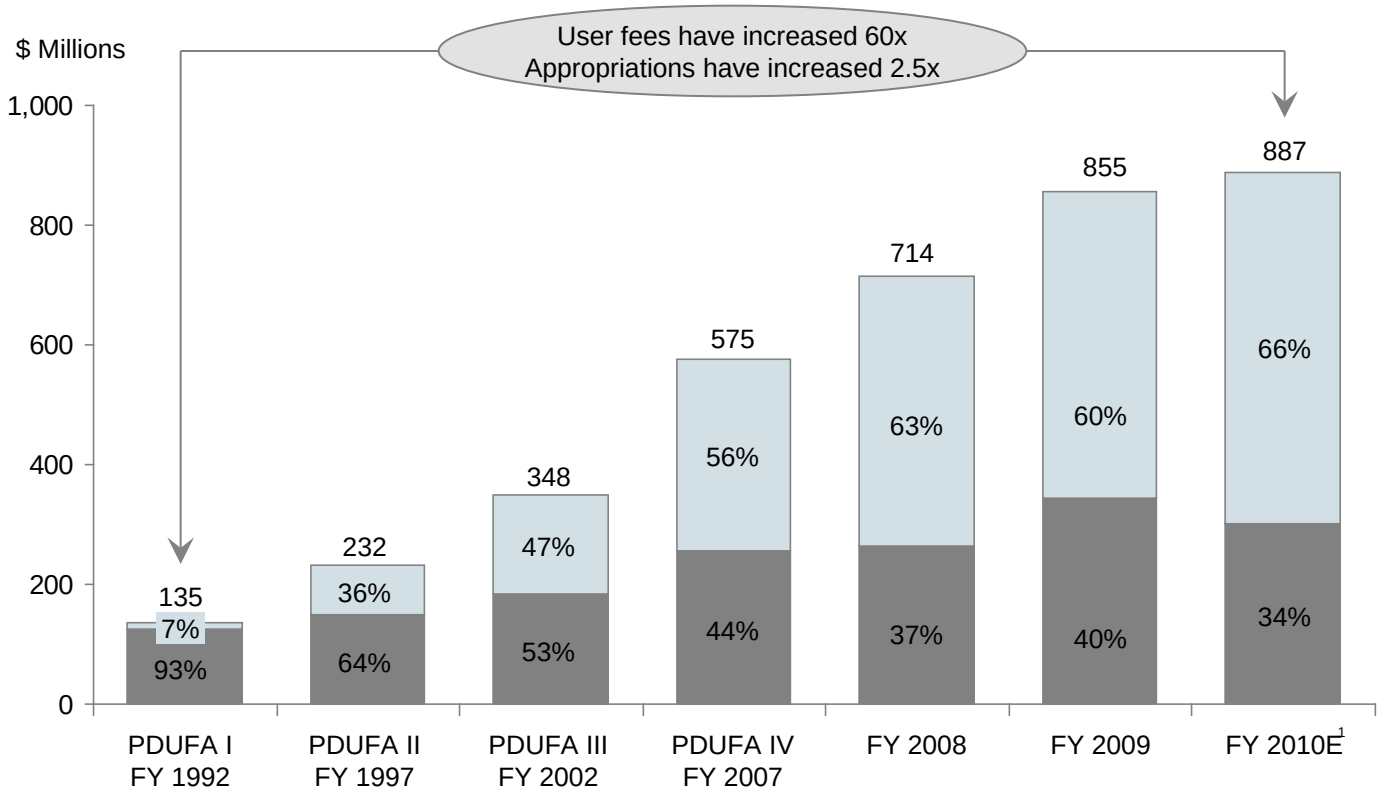
60% Percentage new medicines on the market overseas for ≥1 year before US approval

"Drug lag" became a significant concern for patients, Congress, and biopharmaceutical research companies

Source: FDA: Third Annual Performance Report: Prescription Drug user Fee Act of 1992, Fiscal Year 1995 Report to Congress, December 1, 1995; FDA, FY2011 Performance Report to the President and the Congress for the Prescription Drug User Fee Act.

User fees are intended to supplement, not supplant Congressional appropriations

Human drug review funding includes funds from appropriations and user fees.



User fees: Fees paid by pharmaceutical companies to the FDA

Appropriations: Tax dollars appropriated to the FDA by Congress

Note: Fiscal year in which PDUFA was authorized
1. FY 2010 appropriations estimate based on FY 2009 budget request and FY 2010 increase
Source: FDA PDUFA Webinar; 2009: http://www.hhs.gov/asl/testify/2008/02/t20080227h.html; 2010: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/UCM153491.pdf

PDUFA activities significantly expanded by FDAAA/PDUFA IV

Activities required by PDUFA

PDUFA I 1992	PDUFA II 1997	PDUFA III 2002	PDUFA IV 2007
		FDAAA significantly expanded post-approval safety activities and required Advisory Committees for most new medicines	
		• Post-approval safety activities for 3 years	• Risk Evaluation and Mitigation Strategies • Procedures to analyze drug safety data • Post-approval safety activities for life of drug • Mandatory advisory committees
		• Good Review Management Practices • Improved performance management • Rolling applications	• Good Review Management Practices • Improved performance management • Rolling applications
	• Standards for scheduling meetings • More review guidance	• Standards for scheduling meetings • More review guidance	• Standards for scheduling meetings • More review guidance
• Review goals: – 12 months standard – 6 months priority	• Review goals: – 12/10 months standard – 6 months priority	• Review goals: – 10 months standard – 6 months priority	• Review goals: – 10 months standard – 6 months priority

Review process requirements

Post-approval requirements

Overview of PDUFA-V Performance Goals Letter

- ***Basic structure*** **of the human drug review program, including FDA's high review standards for safety and efficacy, remains unchanged**

- ***New provisions*** **provide FDA with tools to make safe and effective new medicines available to patients in a more efficient, consistent, and timely manner**

Overview of Performance Goals Letter: PDUFA-V Key Enhancements

- **Enhanced review model for New Molecular Entities (NME)**
  - Increases efficiency and predictability
  - Improves upon current review performance* by enhancing scientific communication and feedback
  - Includes independent third party assessment of the Program's effect
- **User fee funding for Regulatory Science, Expediting Drug Development, and Patient Safety**
  - Advance development of drugs for rare diseases
  - Advance FDA capabilities for biomarker qualification, pharmaco-genomics, patient-reported outcomes, and meta-analysis evaluations
  - Promote innovation through enhanced communication
  - Develop and implement structured benefit-risk framework; patient-focused drug development
  - REMS standardization and Sentinel
  - Electronic regulatory submissions (eCTD) and data standards

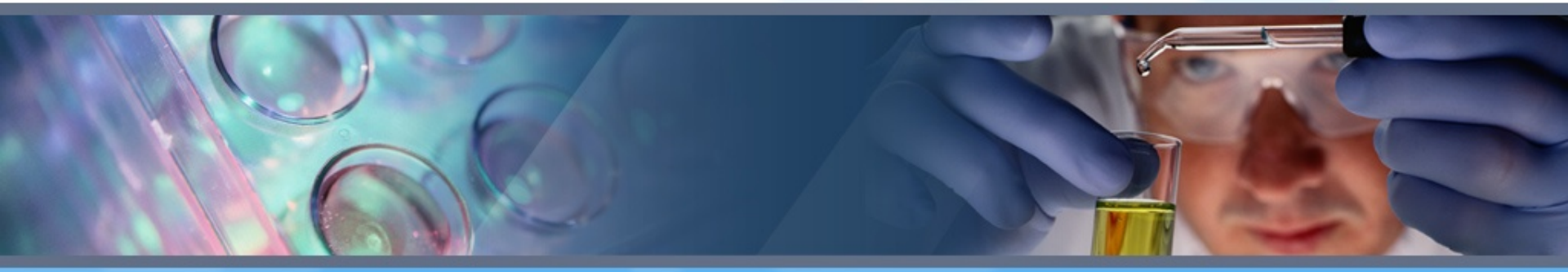
*** FY2010: 9/13 months for priority/standard application; ~35% of application approved in first cycle.**

PDUFA Reauthorization Timeline

Date	Description
May 2011	Final recommendations forwarded to HHS/OMB for vetting and clearance
September 1, 2011	FDA publishes PDUFA-V goals letter on website
October 24, 2011	Public meeting on reauthorization recommendations
December 2011	FDA briefs HHS/OMB on any revisions to recommendations
January 13, 2012	Presentation of final FDA recommendations to Congress
Early Q3 2012	If PDUFA not reauthorized, FDA must send notice of termination letters to ~2,000 employees
September 30, 2012	PDUFA IV expires

PhRMA
New Medicines. New Hope.

Bio
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

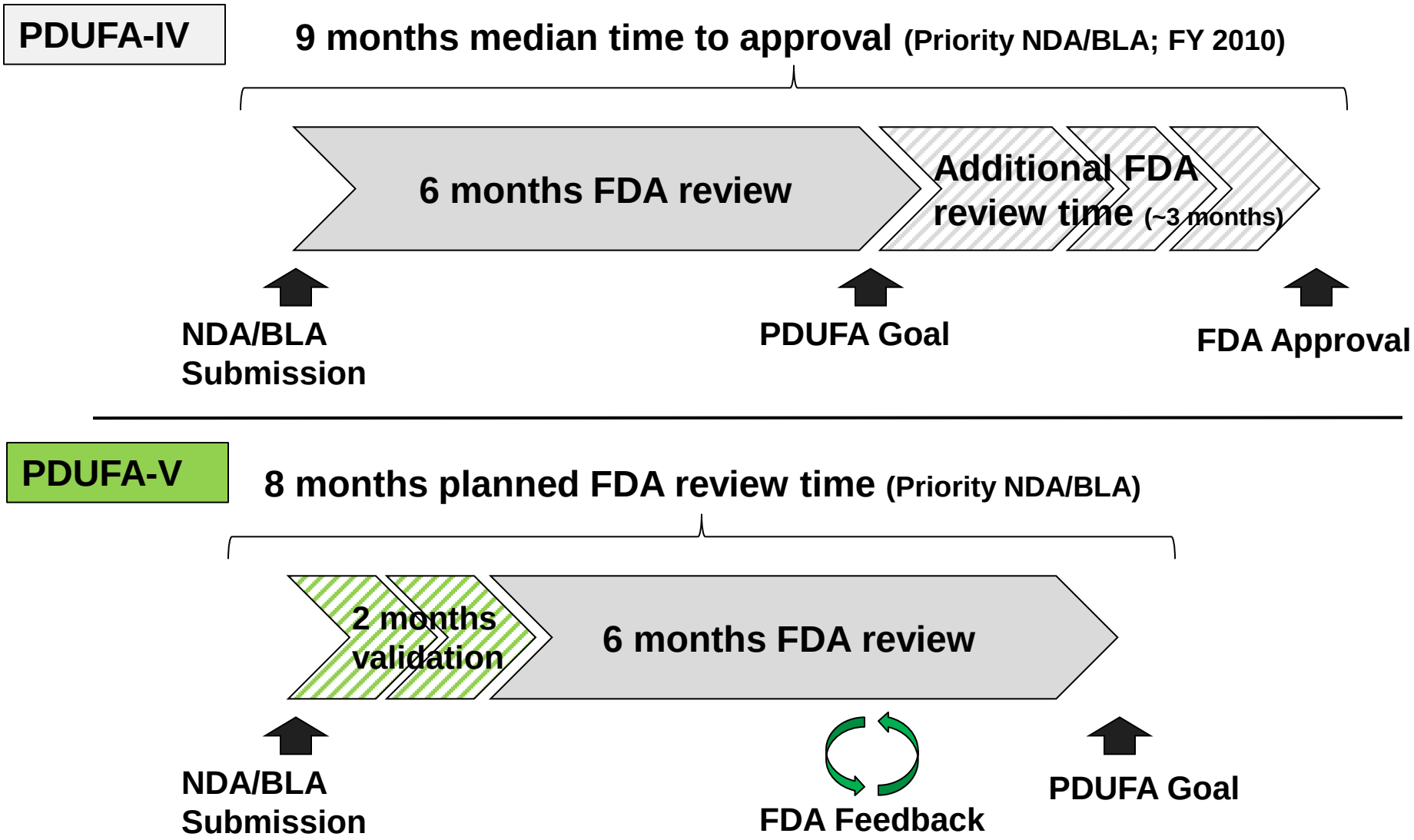


PDUFA-V Reauthorization

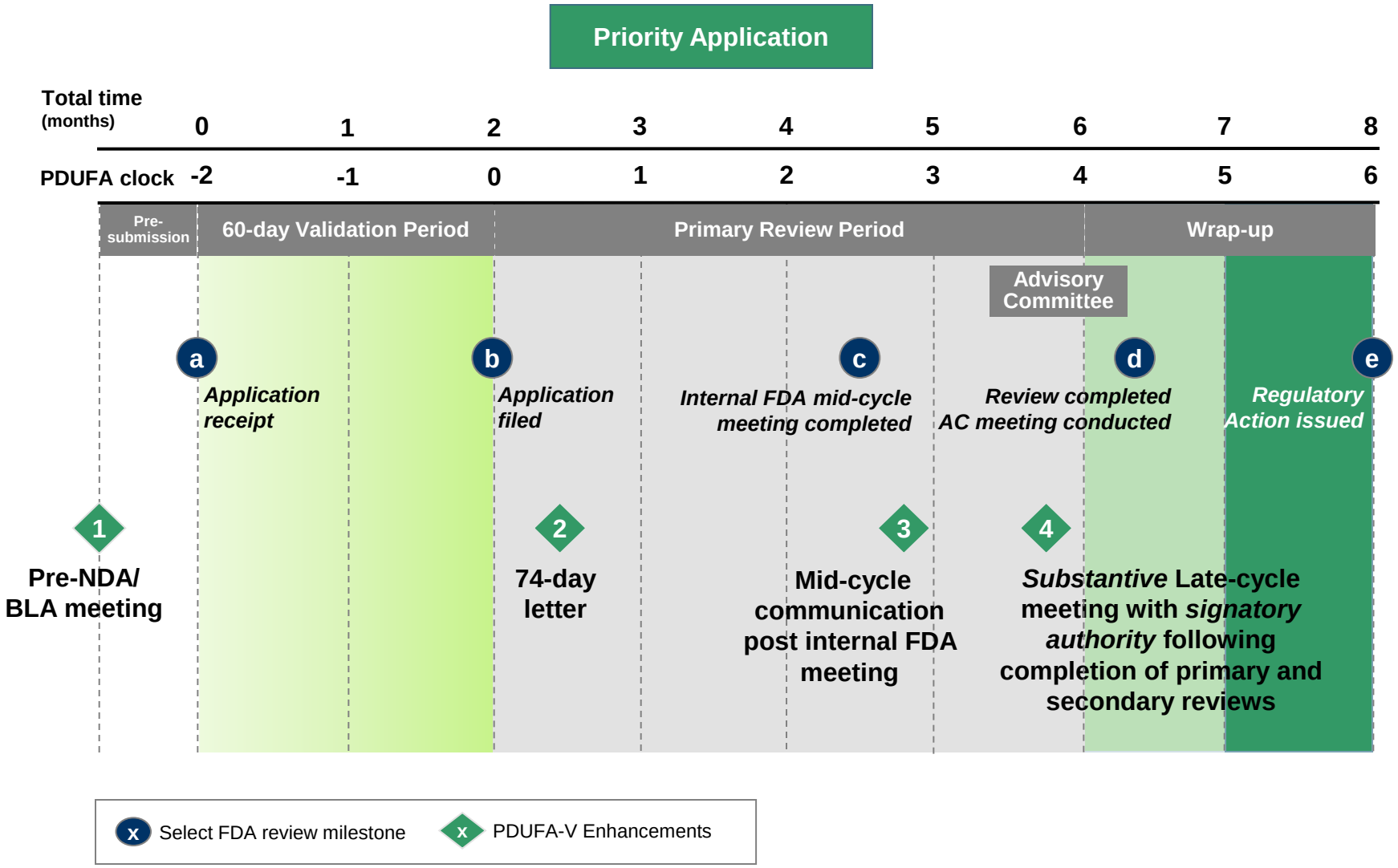
Highlights of Performance Goals Letter

Additional Information

Overview of Performance Goals Letter
Enhanced NME NDA/Original BLA Review Program



Overview of Performance Goals Letter
Enhanced NME NDA/Original BLA Review Program



Overview of Performance Goals Letter
Enhancing Regulatory Science & Patient Safety

Overview of Regulatory Science and Patient Safety Goals
✓ Advance development of drugs for rare diseases
✓ Advance biomarker qualification & pharmacogenomics
✓ Ensure quality of patient-reported outcomes
✓ Ensure quality in meta-analysis
✓ Enhanced FDA/sponsor communications during drug development
✓ Implement Benefit/Risk framework, including patient-focused drug development
✓ REMS standardization & Sentinel
✓ Electronic regulatory submissions (eCTD) and data standards

Overview of Performance Goals Letter
Enhancing Regulatory Science

- **Provides new resources to advance innovative approaches to the development and review of new medicines**
  - Supports the advancement of **drug development for rare diseases** by promoting innovative new therapies and enhancing FDA's ability to regulate drugs & biologics for smaller patient populations
  - Supports FDA staff capacity to review submissions containing issues involving **biomarkers and pharmacogenomics**
  - Advances development and validation of **patient-reported outcomes** (PROs)
  - Supports scientific advancement of **meta-analysis** by providing resources for FDA to explore scientifically valid methods, standards, and potential limitations of meta-analysis, through a public process.
    - This effort will enhance FDA's drug safety efforts by improving the agency's ability to consistently analyze large pre- and post-market data sets

Overview of Performance Goals Letter
Enhancing Regulatory Science

- **Promoting Innovation Through Enhanced Communication Between FDA and Sponsors During Drug Development**
  - Timely interactive communication with sponsors during drug development is a core Agency activity to help achieve the Agency's mission to facilitate the conduct of efficient and effective drug development programs, which can enhance public health by making new safe and effective drugs available to the American public in a timely manner
    - Dedicated drug development communication and training staff
    - Draft guidance for industry
    - Identification and dissemination of best practices for enhanced communication

Overview of Performance Goals Letter
Enhancing Benefit/Risk Assessments

- **Enhance FDA's regulatory decision-making process and transparency through the development and implementation of a structured Benefit/Risk framework**
  - Full public process, including public meetings and opportunities for commenting
  - Will help ensure that FDA's regulatory decisions are based on the best available methods and facilitate the balanced consideration of the benefits and risk of new medicines
  - The effort will also help to communicate regulatory decisions in a way that will improve public understanding of the agency's work

Overview of Performance Goals Letter
Enhancing Drug Safety

- **The PDUFA-V performance goals letter includes important provisions to further enhance FDA's robust drug safety system**
  - **Risk Evaluation and Mitigation Strategies (REMS)**
    - Standardize and better integrate REMS-related activities into FDA's review process and the healthcare system with the goal of reducing the burden of REMS on patients and healthcare providers
    - Provides for an assessment of the effectiveness of risk evaluation and mitigation strategies (REMS)
  - **Sentinel**
    - Supports efforts to continue to develop the use of Sentinel to enhance FDA's capacity for active drug safety surveillance
    - Modernizes pharmacovigilance activities by maximizing the utility of tools FDA uses for adverse event detection and risk assessment
  - **Standardized Electronic Regulatory Submissions**
    - Improve the efficiency of FDA's human drug review program and enhance FDA's ability to explore safety signals