Investment case for Regulatory Systems Strengthening: PDUFA/GDUFA

Khyati Roberts, R.Ph., Senior Director
Regulatory Policy & Intelligence, AbbVie

On behalf of FIFARMA

Disclaimer

This presentation does not constitute regulatory or legal advice by AbbVie or any of its subsidiaries. Please consult with your legal advisors for assistance in interpreting and complying with any pertinent laws or regulations.

Outline

- Overview of Prescription Drug User Act (PDUFA)
- Overview of Generic Drug User Fee Act (GDUFA)
- Criteria for Successful User Fee Programs

History of PDUFA Legislation

- **PDUFA I: Reducing Application Review Time (FY 1993 to FY 1997)**
  - Established fee structure for premarket review; reduced backlog; set predictable timelines for review action
- **PDUFA II: Facilitating the Drug Development Process (FY 1998 to FY 2002)**
  - Shortened review performance level commitments;
  - New procedural goals improve communication between FDA and sponsors
- **PDUFA III: Refining the Process - From Drug Development to Application Review to Postmarket Surveillance (FY 2003 to FY 2007)**
  - Significant added funding
  - Increased FDA-sponsored interactions during drug development and application review
  - Use of user fees for certain aspects of postmarket risk management for up to three years after approval
- **PDUFA IV: Enhancing Drug Safety (FY 2008 to FY 2012)**
  - Increased and stabilized base funding
  - Enhanced premarket review
  - Created a modern postmarket safety system
- **PDUFA V: Innovation and Modernization in the Drug Review Process (FY 2013 to FY 2017)**
  - Small increase to base funding
  - Addition of the "program" to enhance the review of new molecular entities and biologics
  - Increases the utilization of the electronic submissions system

PDUFA VI is currently under active negotiations as it must be reauthorized by October 1, 2017

Key Elements of PDUFA

- Collection of Fees for:
  - Application fees: Due when a sponsor submits a New Drug Application (NDA) or Biologics License Application (BLA)
  - Product fees: Annual fee for marketed drugs for which no generic versions are approved
  - Establishment fees: Annual fee for each manufacturing site that manufactures at least one approved prescription drug for which no generic versions are approved
- User fees supplement, but do not replace, Congressional appropriations
- Funds dedicated to improvement of review process
- Establishment of key performance goals, e.g., review timelines

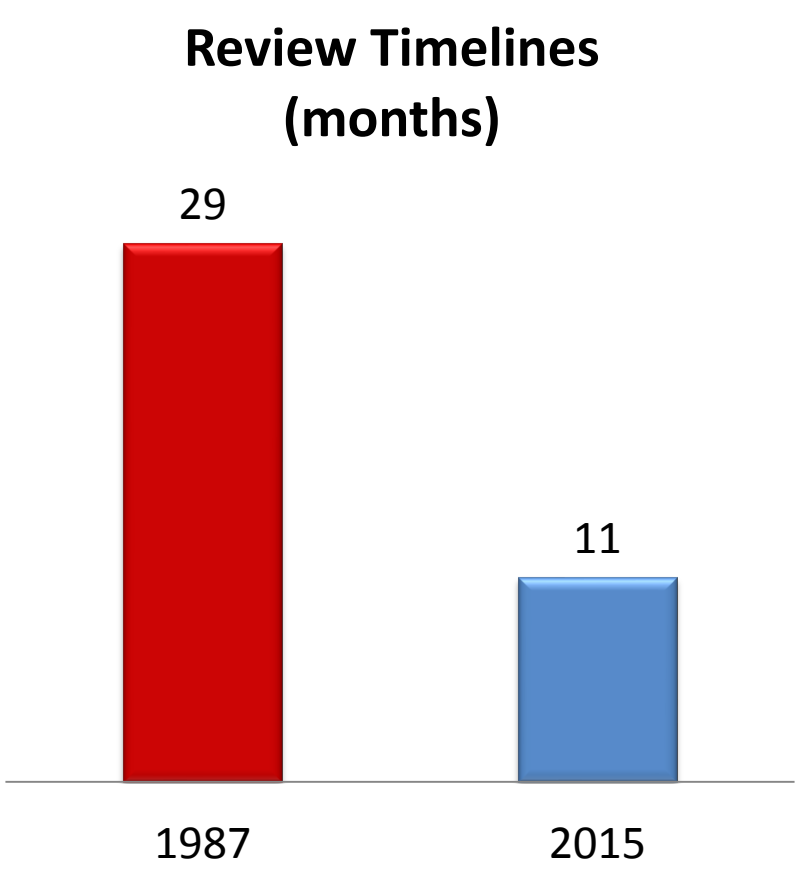
PDUFA V Performance Goals

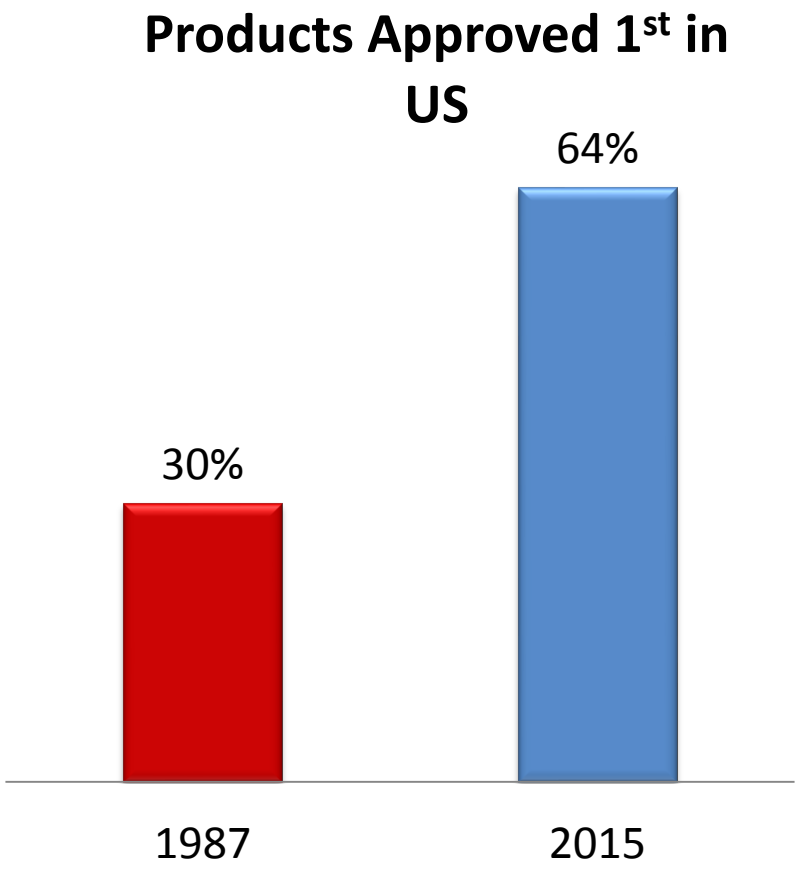
Currently over 30 specific performance goals

KEY EXAMPLES	STANDARD	PRIORITY
NME NDAs and original BLAs	90% in 10 months of the 60 day filing date	90% in 6 months of the 60 day filing date
Non NME NDAs	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmissions	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmissions	90% in 6 months of the receipt date	90% in 6 months of the receipt date
Original Efficacy Supplements	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmitted Efficacy Supplements	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmitted Efficacy Supplements	90% in 6 months of the receipt date	90% in 6 months of the receipt date
	PRIOR APPROVAL	**ALL OTHER**
Manufacturing Supplements	90% in 4 months of the receipt date	90% in 6 months of the receipt date

US Review Timeline History

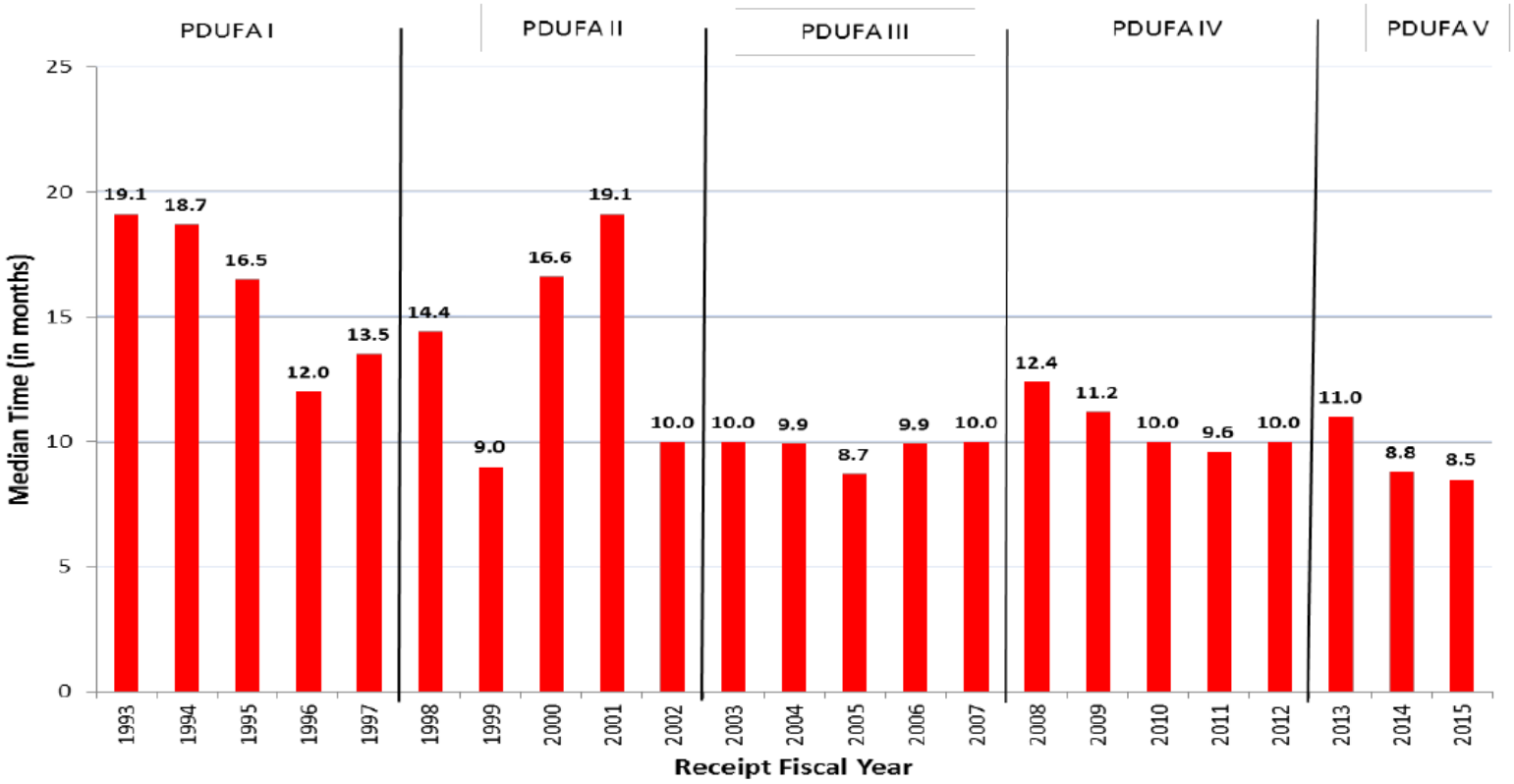
In the late 1980's, the U.S. lagged other countries in drug approvals





FDA/CDER NME Median Total Time to Approval

Source: FDA Presentation from John Jenkins at the FDA CMS Summit, December 14, 2015 (Data as of 12/9/2015)



Data as of 12/9/2015

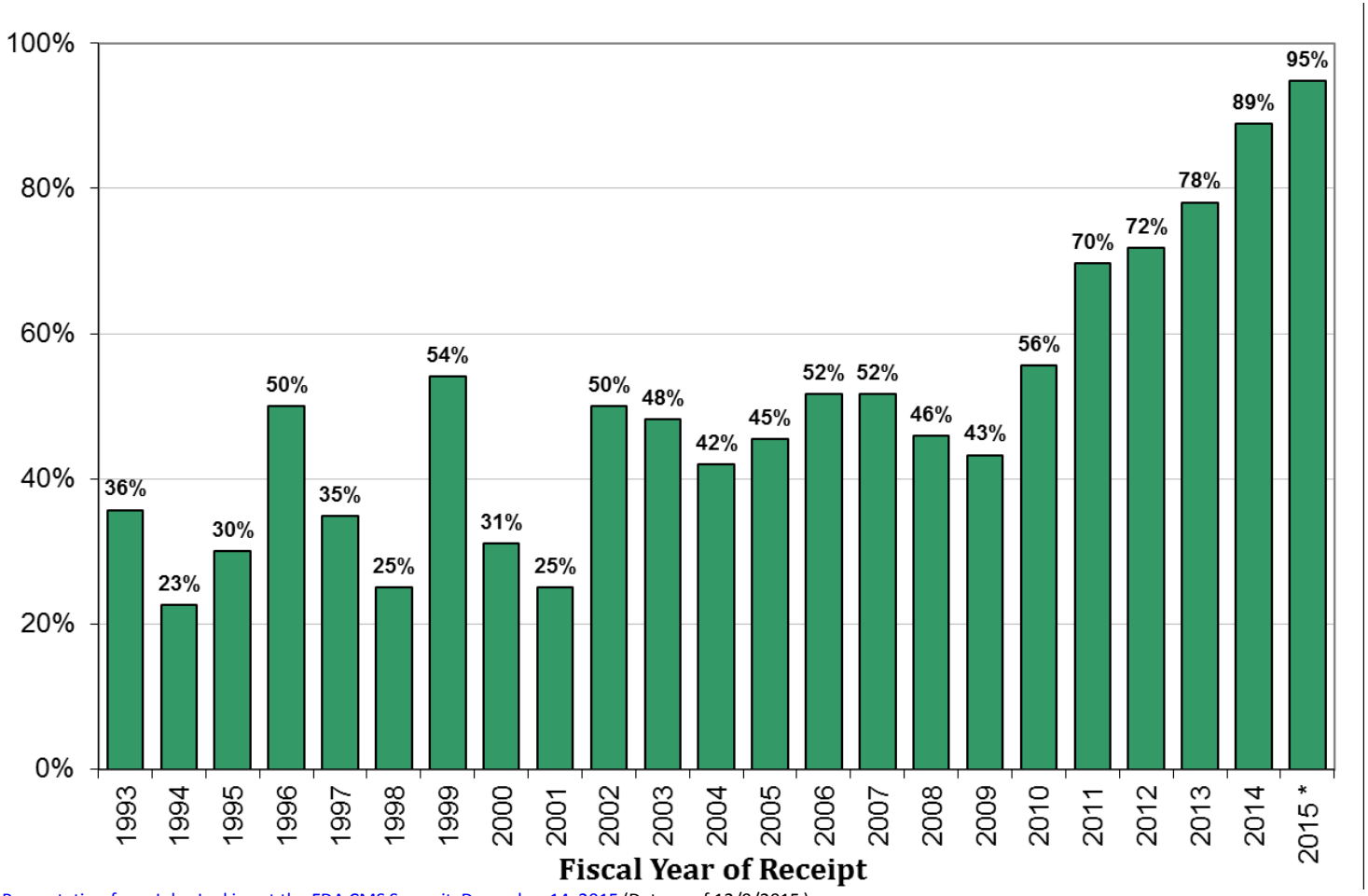
† Original BLAs that do not contain a new active ingredient are excluded.

SALUD
SECRETARÍA DE SALUD

Cofepris
Comisión Federal para la Protección contra Riesgos Sanitarios

PANDRH
Pan American Network for Drug Regulatory Harmonization
Pan American Health Organization
World Health Organization
Americas

FDA/CDER 1st Action Approval Rates



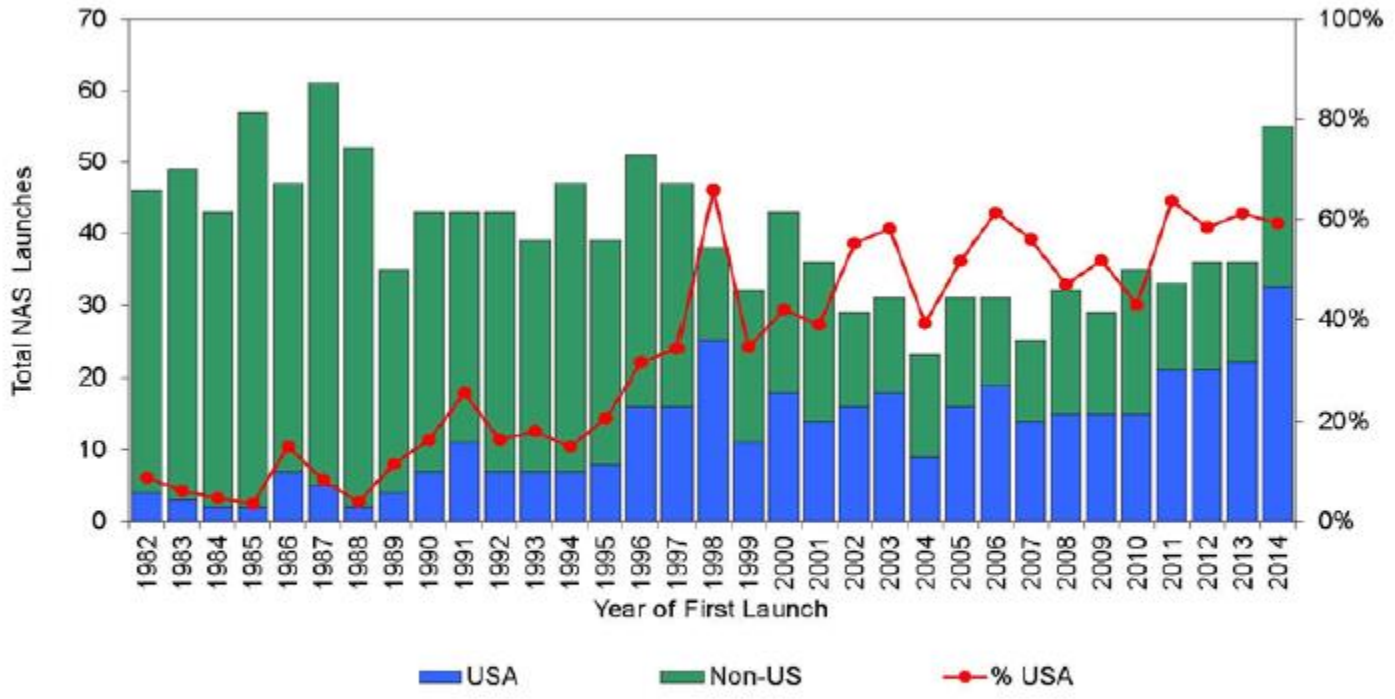
Source: FDA Presentation from John Jenkins at the FDA CMS Summit, December 14, 2015 (Data as of 12/9/2015)

† Multiple applications pertaining to a single new molecular/biologic entity (e.g., single ingredient and combinations) are only counted once. Therefore, the numbers represented here for filings are not indicative of workload in the PDUFA V Program.

† Original BLAs that do not contain a new active ingredient are excluded. Percentages exclude pending applications from the denominator.

* FY 15 Cohort has 25 pending applications.

Trends on US Share of Active New Substances on Global Market



Data as of 11/30/2015

Source: *Scrip Magazine* (1982 - 2006), *Pharmaprojects/Citeline* **Pharma R&D Annual Review** (2007 - 2014)

Source: FDA Presentation from John Jenkins at the FDA CMS Summit, December 14, 2015 (Data as of 12/9/2015)

History of GDUFA Legislation

- Backlog of generic drug applications was increasing
- Enacted into law on July 9, 2012, to increase staffing and create more efficiencies
- User fees supplement, but do not replace, Congressional appropriations
- Funds dedicated to improvement of review process and enhance surveillance inspections
- Collection of reasonable fees for:
  - Application Fees
  - Supplement Fees
  - Drug Master File Fees
  - Facility Fees
  - Backlog Application Fees
- Milestones Established
  - Application metrics
  - Backlog metrics
  - Inspection metrics
  - Efficiency Enhancements
  - Regulatory Science Initiatives

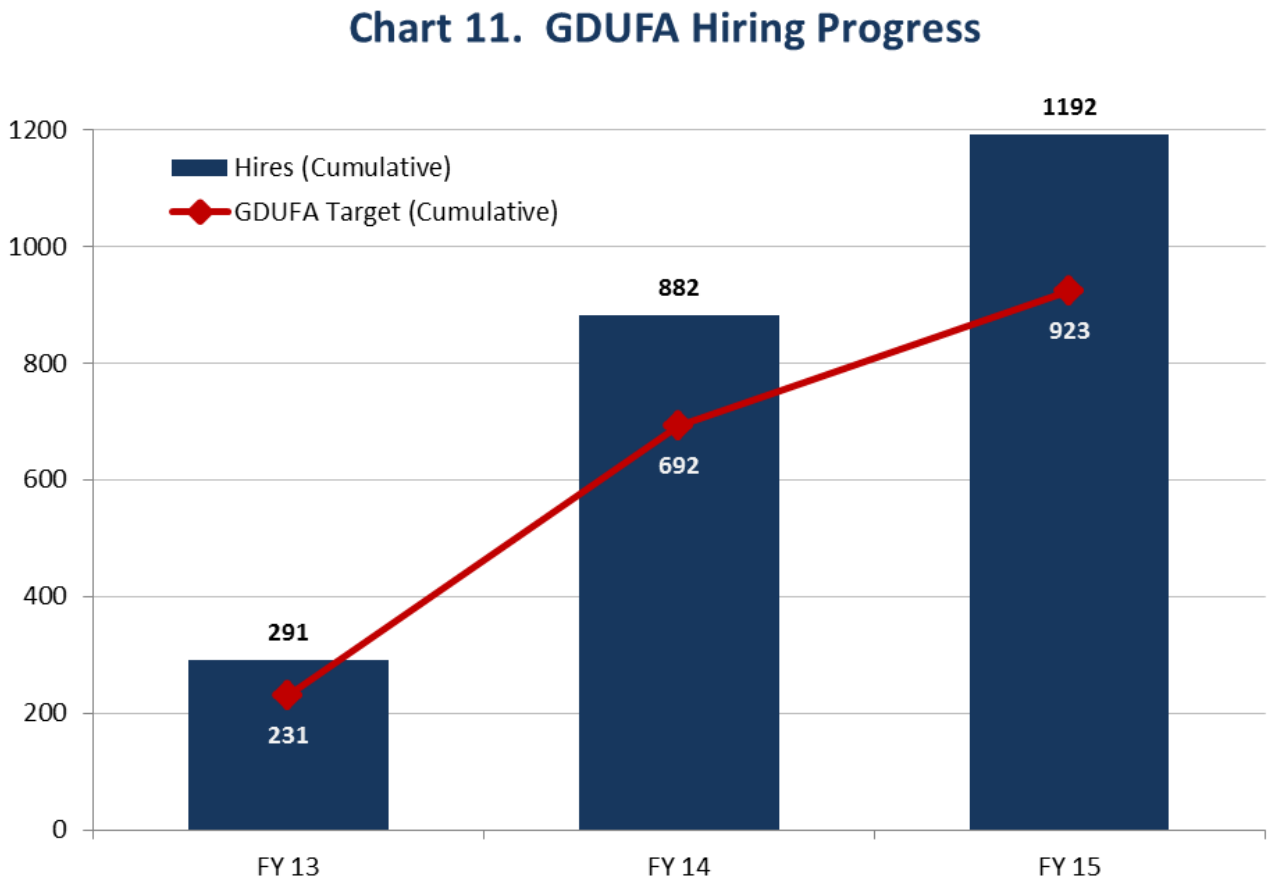
Current GDUFA Performance Goals

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Original ANDA	Expedited review of paragraph VI and maintain pre-GDUFA productivity		60% in 15 months	75% in 15 months	90% in 10 months
Tier 1 Major Amendment	Phased in Goals		60% in 10 months	75% in 10 months	90% in 10 months
Tier 1 Minor Amendment (1st-3rd)			60% in 3 months*	75% in 3months*	90% in 3months*
Tier 1 Minor Amendment (4th – 5th)			60% in 6 months*	75% in 6 months*	90% in 6 months*
Tier 2 Amendment			60% in 12 months	75% in 12 months	90% in 12 months
Prior Approval Supplement			60% in 6 months*	75% in 6 months*	90% in 6 months*
Backlog (ANDAs, amendments, PAS)	Act on 90% by end of FY 2017				
Controlled Correspondences	Phased in Goals		70% in 4 months**	70% in 2 months**	90% in 2 months

*10 months if inspection required
**1 additional month if clinical input needed

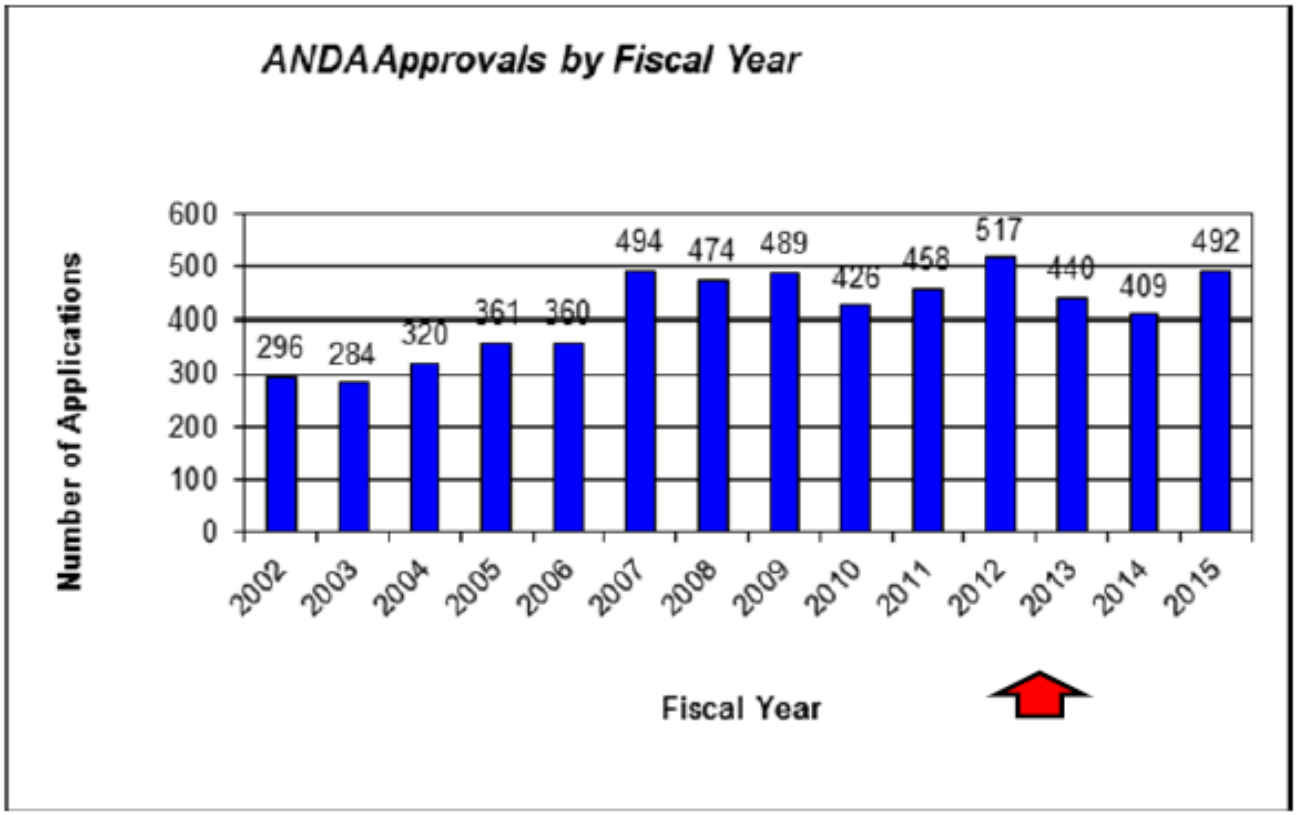
Increased Review Staff

Source: Office of Generic Drugs Director's Update, GPhA Annual Meeting, February 23, 2016



Maintaining Productivity

Source: Office of Generic Drugs Director's Update, GPhA Annual Meeting, February 23, 2016

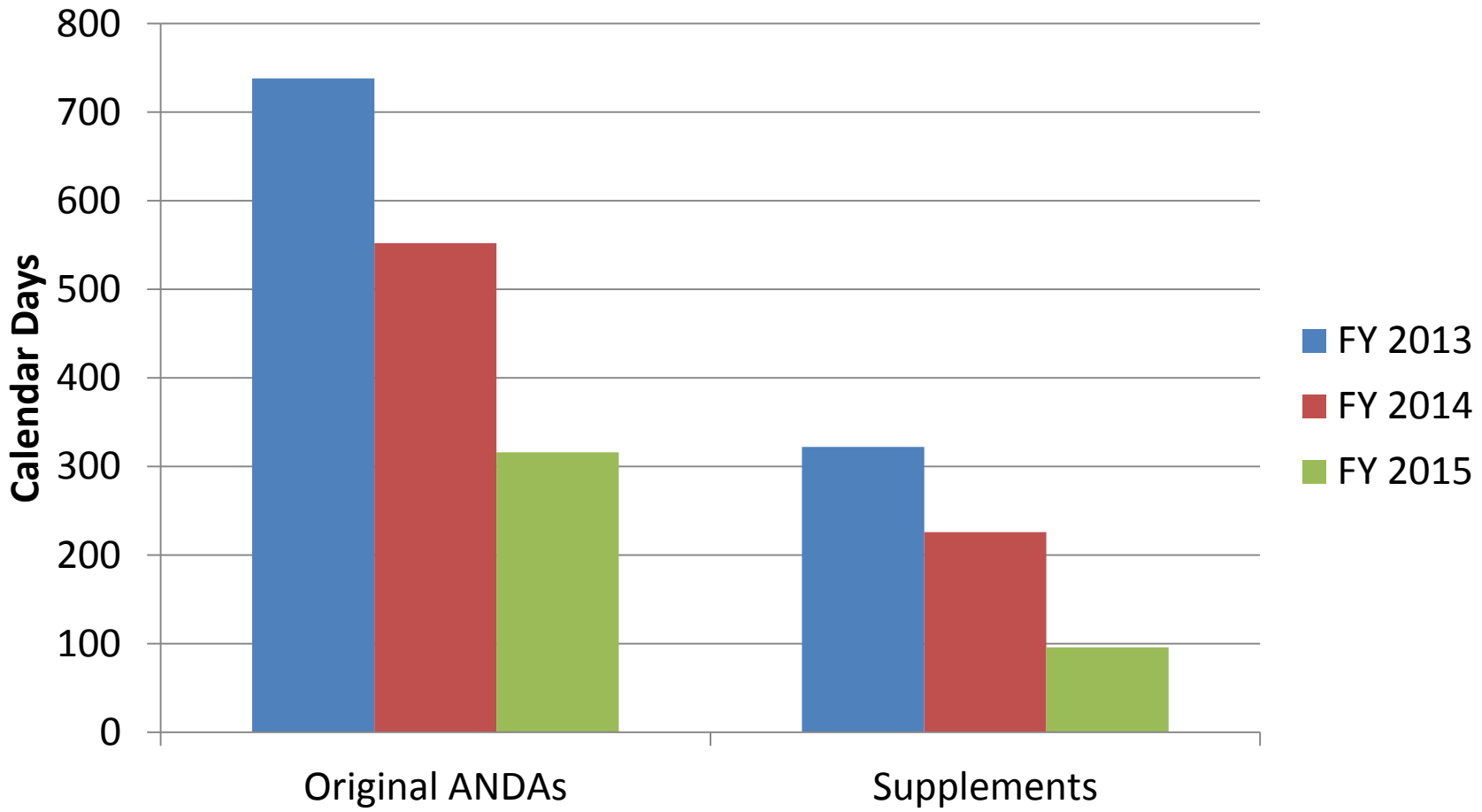


** FDA will aspire to the extent possible to **maintain levels of productivity at least similar to pre-GDUFA levels**, while hiring and training incremental staff necessary to achieve the program performance goals, building necessary systems and implementing outlined program changes in years 1 and 2 of the program (GDUFA Commitment Letter, page 3)

*Numbers are based on current data and will be further scrubbed for formal reporting purposes

Decreased Approval Times

Source: FY 2015 FDA GDUFA Performance Report



Criteria for Successful User Fee Programs (1 of 2)

- Industry-Regulatory Authority negotiate milestones
- User fees must be dedicated for review enhancements
- Communication between sponsors/health authority is key to success in drug development
- Transparency, Predictability and Accountability
- Phased in performance goals

Criteria for Successful User Fee Programs (2 of 2)

- Infrastructure to support increased staff
- Important to include all stakeholders in the conversation
- Fees must be reasonable
- Industry must submit high quality applications
- Avoid addition of unfunded mandates

SALUD
SECRETARÍA DE SALUD

Cofepris
Comisión Federal para la Protección contra Riesgos Sanitarios

PANDRH
Pan American Network for Drug Regulatory Harmonization

Pan American Health Organization

World Health Organization
Americas