Keynote:
Generic Drug Program Update

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Director, Office of Generic Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Outline

1. Introduction
2. Generic Drug Program Overview
3. Generic Drug User Fee Amendments (GDUFA)
4. Drug Competition Action Plan (DCAP)
5. Conclusion

Introduction

- FDA Office of Generic Drugs, CDER
- FDA Office of Study Integrity and Surveillance, Office of Translational Sciences (OTS), CDER
- PAREXEL Consulting
- FDA Office of Clinical Pharmacology, OTS, CDER
- Pfizer, Ann Arbor, MI
- BMS, Princeton, NJ
- University of Michigan, Ann Arbor, MI

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Generic Drug Program Overview

Office of Generic Drugs (OGD)

Director:
Sally Choe, PhD

Deputy Director:
Howard Chazin, MD (Acting)

Office of Research and Standards (ORS)

Director:
Rob Lionberger, PhD

Deputy Director:
Lei Zhang, PhD

- Division of Therapeutic Performance
- Division of Quantitative Methods & Modeling

Office of Bioequivalence (OB)

Director:
Dale Conner, PharmD

Acting Deputy Director:
Ethan Stier, PhD

- Division of Bioequivalence I
- Division of Bioequivalence II
- Division of Bioequivalence III
- Division of Clinical Review

Office of Generic Drug Policy (OGDP)

Director:
Maryll Toufanian, JD

Deputy Director:
Kristin Davis, JD

- Division of Legal and Regulatory Support
- Division of Policy Development

Office of Regulatory Operations (ORO)

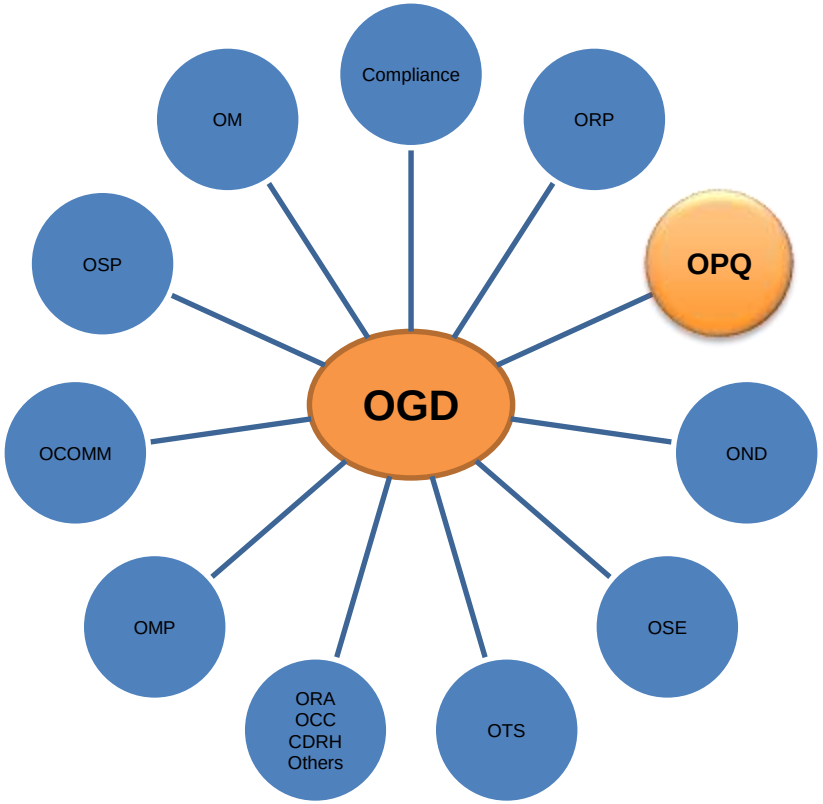
Director:
Edward (Ted) Sherwood

Deputy Director:
CDR Vincent Sansone, PharmD

- Division of Labeling Review
- Division of Filing Review
- Division of Project Management
- Division of Quality Management Systems

U.S. FDA Generic Drug Program

- Abbreviated new drug applications (ANDAs) involve multiple offices within FDA
  - OGD issues regulatory action on ANDAs
  - Office of Pharmaceutical Quality (OPQ) and OGD collaborate on technical review of ANDAs
- Many offices across CDER and FDA contribute to program success



Generic Drug Program

Generic Drug User Fee Amendments (GDUFA)

GDUFA

- Reflects negotiated agreements with industry
- Goals based on assessment of program activities
- GDUFA I (2012)
- GDUFA II (2017)
  - GDUFA II Commitment Letter
  - www.fda.gov/GDUFA

GDUFA II Features

I. Submission Review Performance Goals

II. Original ANDA Review Program Enhancements

III. Pre-ANDA Program and Subsequent Mid-Review-Cycle Meetings for Complex Products

IV. DMF Review Program Enhancements

V. Facilities

VI. Enhanced Accountability and Reporting

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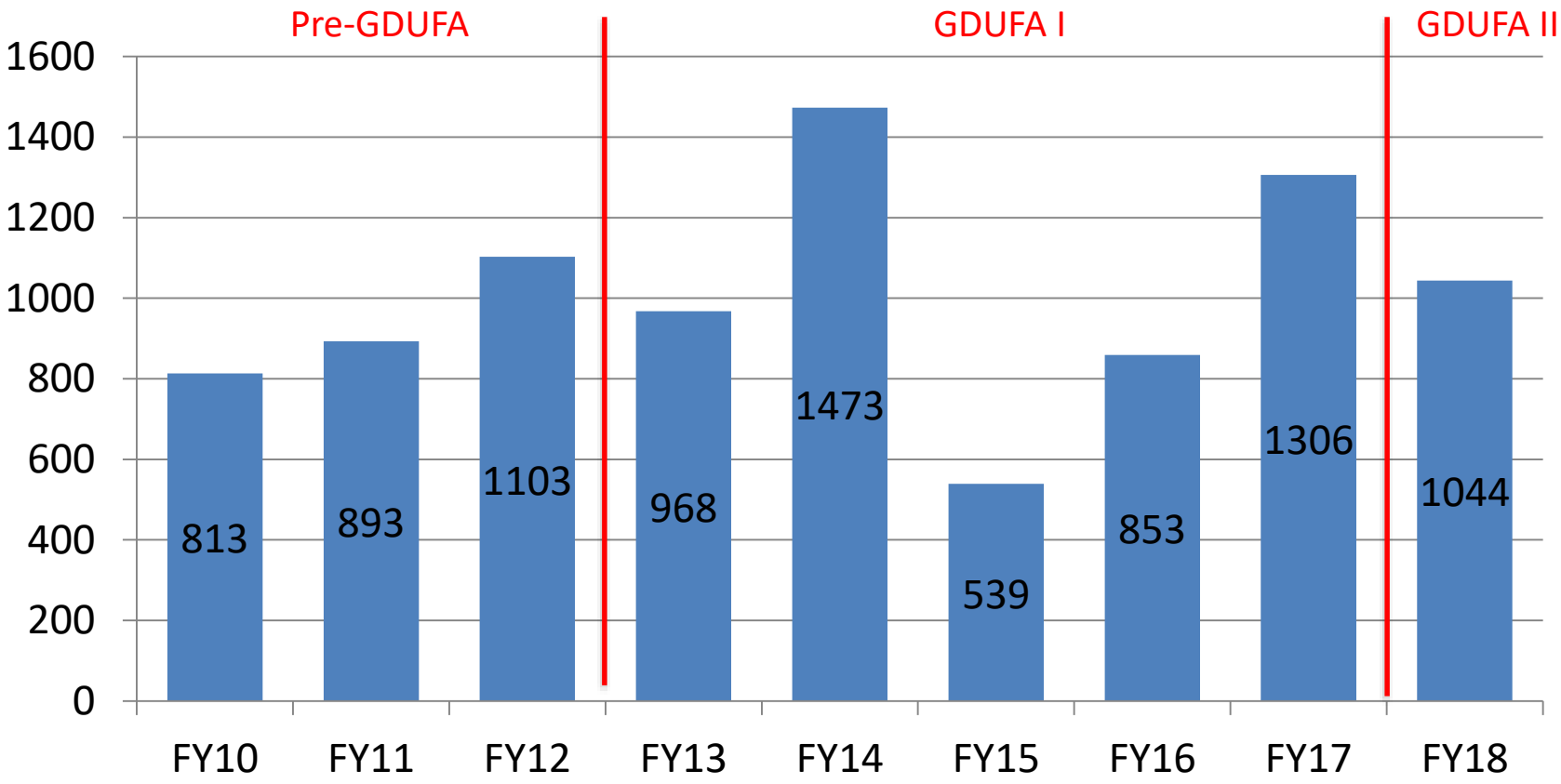
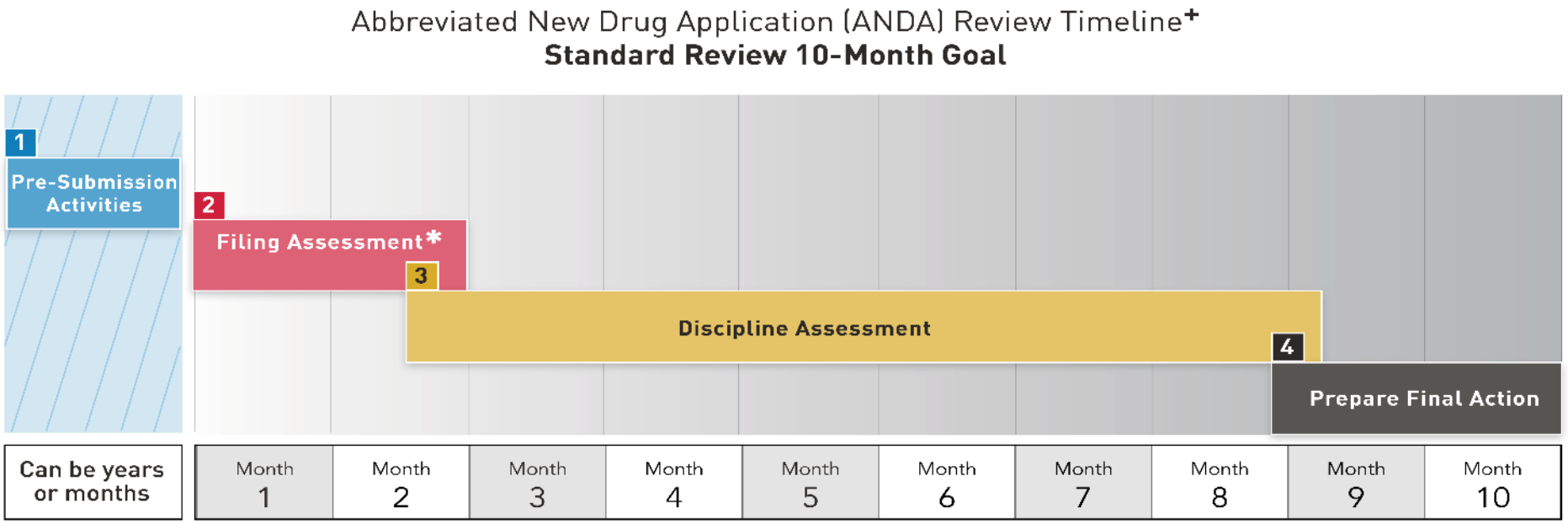
GDUFA Program Performance

ANDA Receipts (Originals)

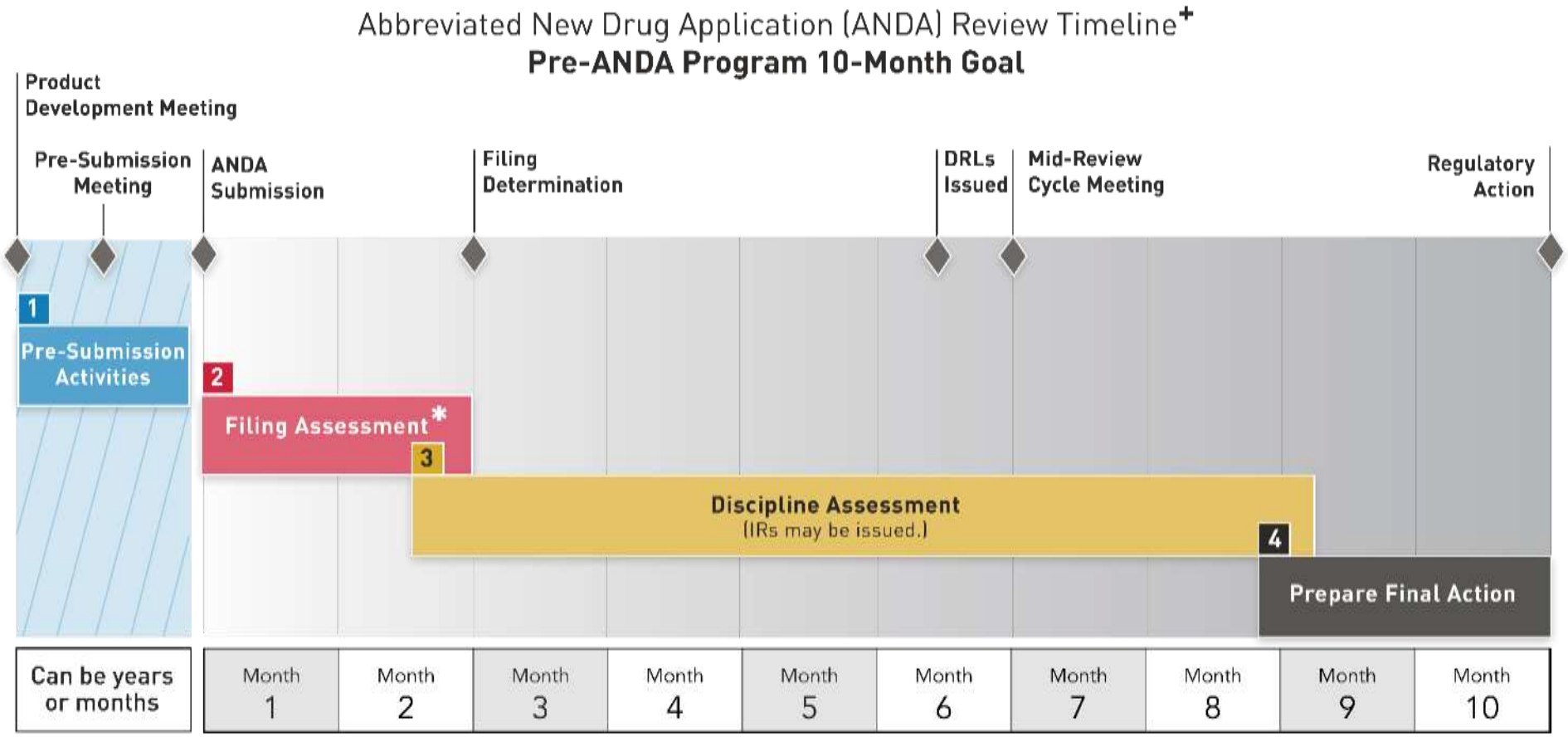


Predictability



+ Each ANDA assessment progresses in a unique and iterative way. This is one example and is not reflective of every ANDA assessment.

* Good ANDA Assessment MAPP



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* Good ANDA Assessment MAPP

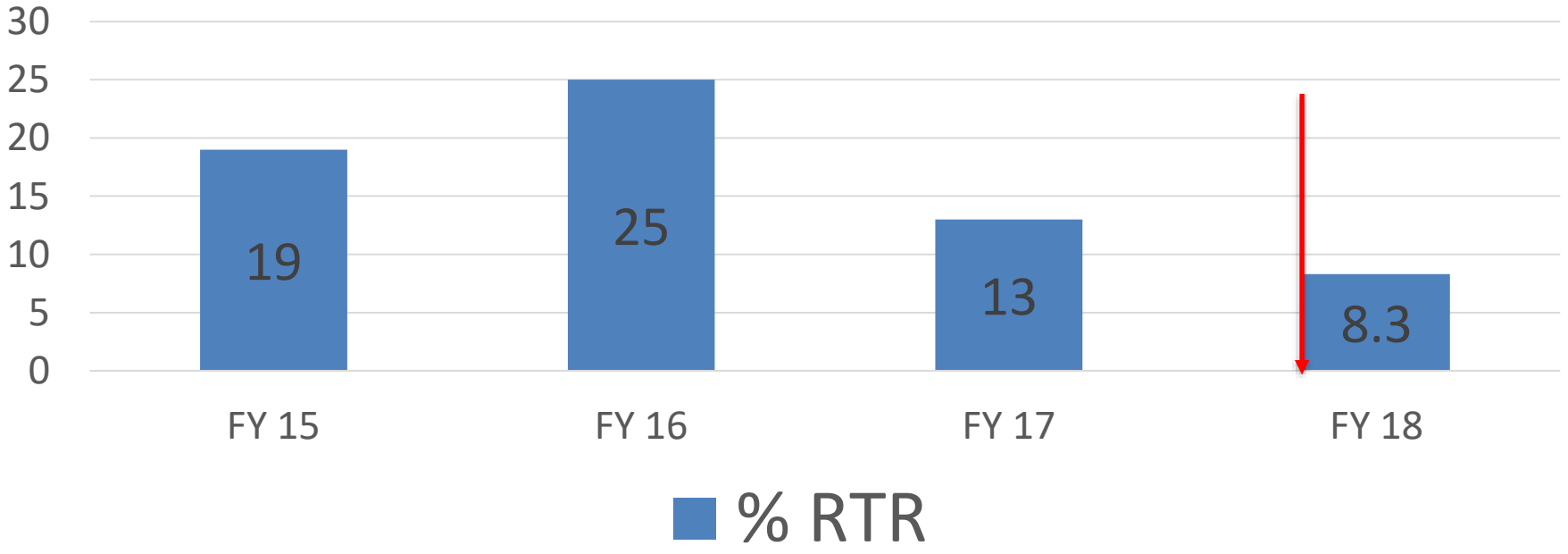
Regulatory Actions

Under GDUFA, FDA has committed to take regulatory actions by the goal date:

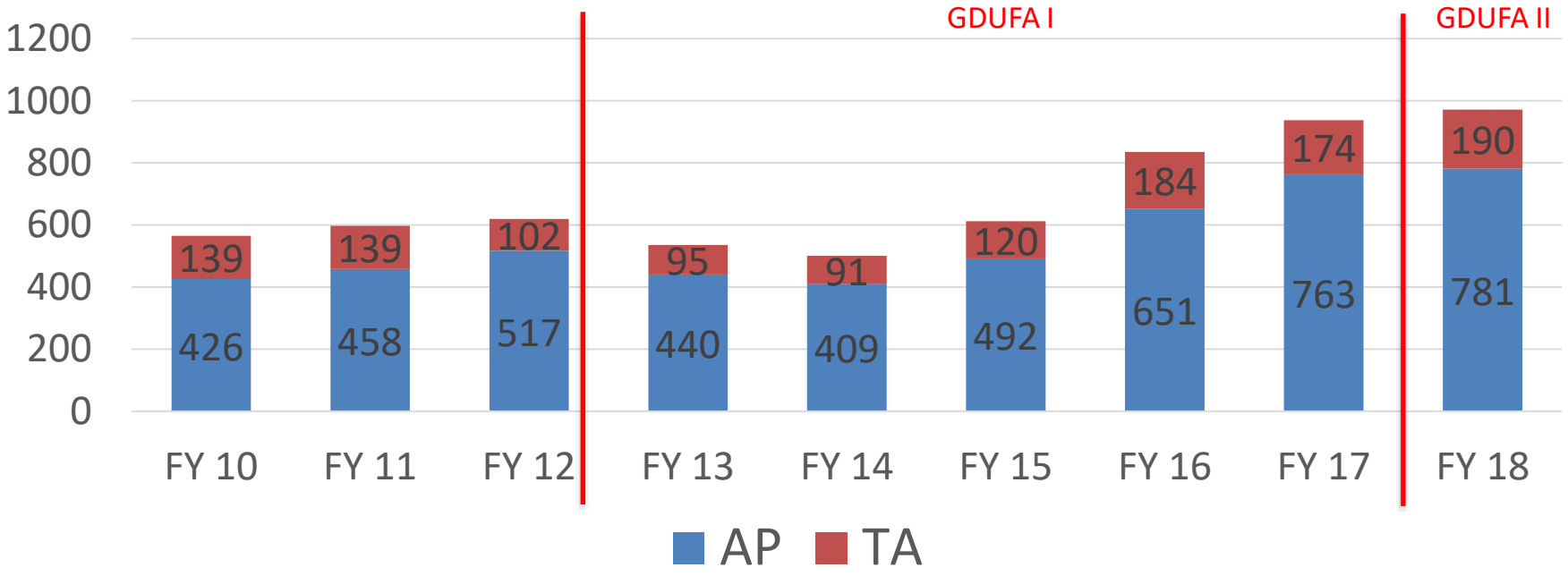
1. Approval (AP)
2. Tentative Approval (TA)
3. Complete Response Letter (CR or CRL)

Filing - Refuse to Receive (RTR)

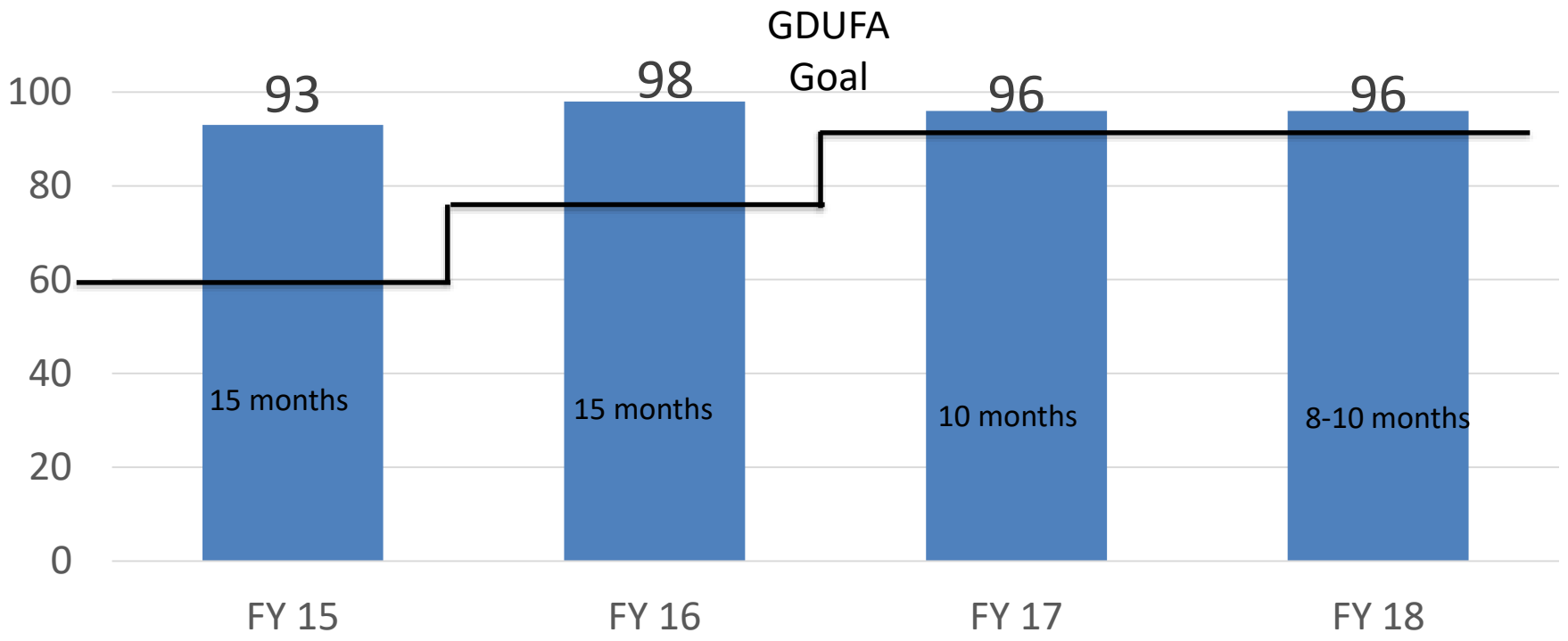
(based on cohort year of submission)



Approval and Tentative Approval Totals



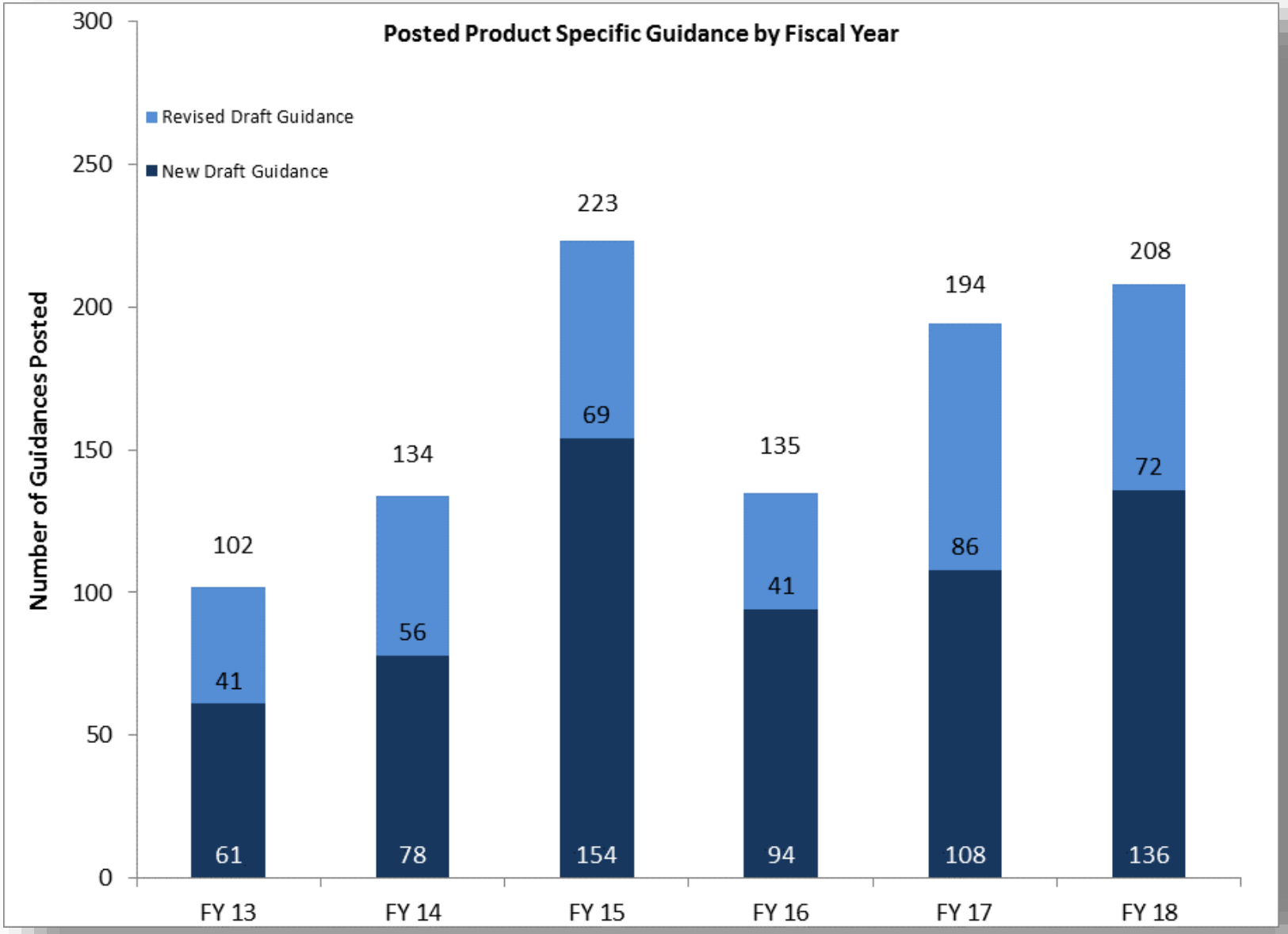
GUDFA Performance – Originals
(new applications)



Product-Specific Guidance (PSG)

- PSGs provide detailed advice on the evidence recommended to demonstrate bioequivalence for a particular RLD
- They support the high first-cycle adequate rate for the bioequivalence sections of ANDAs
- The PSGs web page contains almost 1700 PSGs and new guidances are added every quarter

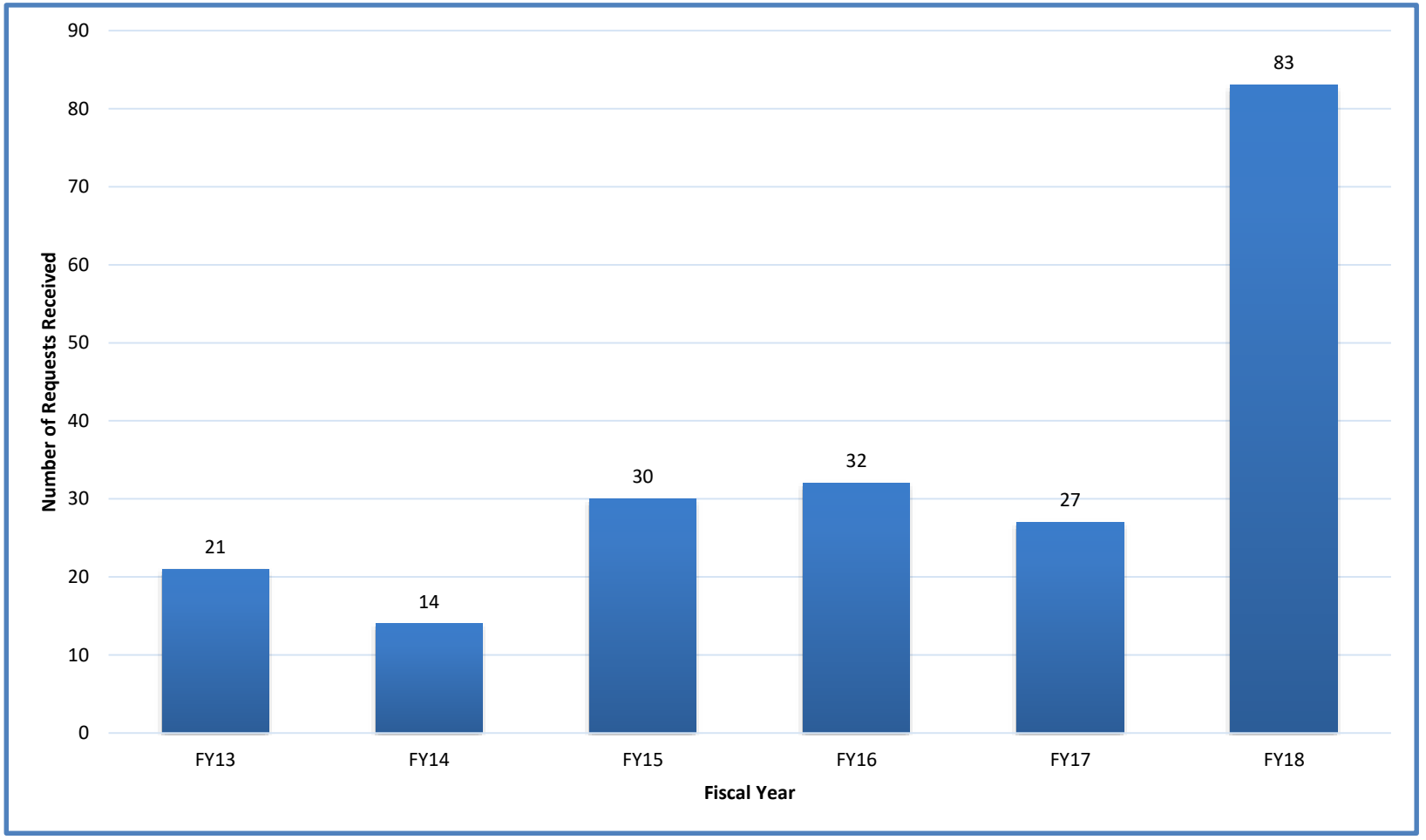
Product-Specific Guidance



Pre-ANDA Meetings for Complex Generics

- Pre-ANDA meetings have new GDUFA II commitments and timelines
- Provide opportunities to discuss new or alternative bioequivalence approaches for complex products
  - Focus on content not covered by PSGs

Pre-ANDA Meeting Requests



Pre-ANDA Meeting Requests – Fiscal Year 2018

Task	Target	Actual
Grant or Deny Meeting within 30 Days	90%	99%
Hold Meeting or Written Response within 120 Days	60%	100%
Send Meeting Minutes within 30 Days	N/A	100%

GDUFA Science and Research

- Provides the scientific foundation for recommendations on complex products
  - Essential for pre-ANDA meetings and product-specific guidance development
- In 2018, GDUFA funded >$14M in OGD regulatory science research programs
  - 24 new contracts and grants
  - 75 ongoing research collaborations
- Visit www.fda.gov/gdufaregscience for more details

Input into Research Priorities

- The GDUFA Research program is focused on challenges to generic product development or assessment

- Stakeholder input was considered to develop the FY19 GDUFA Regulatory Science Priorities:
    1. Complex active ingredients, formulations, or dosage forms
    2. Complex routes of delivery
    3. Complex drug-device combinations
    4. Tools and methodologies for BE and substitutability evaluation

- Your input will determine FY20 priorities
  - 2019 Regulatory Science Initiatives Public Workshop will be held on Wednesday, May 1, 2019 on the White Oak Campus

Additional Fiscal Year 2018 Program Highlights

- Timely and successful update of Orange Book to reflect marketing status updates as required by FDARA
- Competitive generic therapy (CGT) designation and exclusivity requests
- Drug Competition Action Plan (DCAP)

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Drug Competition Action Plan (DCAP)

DCAP Actions

- Commissioner announced in June 2017

- DCAP focuses on:
  - **Improving the efficiency** of generic drug development, review, and approval processes
  - **Maximizing scientific and regulatory clarity** with respect to generic drugs for **complex products**
  - **Closing loopholes** that allow brand drug companies to "game" the system in ways that thwart generic competition

Improving the Efficiency of Generic Drug Development, Review, and Approval

- Good ANDA Submission Practices Draft Guidance
- Good ANDA Assessment Practices MAPP
- ANDA Submissions--Amendments to Abbreviated New Drug Applications Under GDUFA Final Guidance

Maximizing Scientific and Regulatory Clarity for Complex Generic Drug Products

- Issued 76 PSGs for complex generics in 2018
- Published two guidances for industry:
  - Assessing Adhesion with Transdermal and Topical Delivery Systems for ANDAs Revised Draft Guidance
  - Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs Draft Guidance

Closing Loopholes that Allow Brand Drug Companies to "Game" the System

- In May 2018, FDA published a list of drug products about which FDA has received inquiries related to reference listed drug access
- In June 2018, FDA published two draft guidances:
  - Development of a Shared System REMS
  - Waivers of the Single, Shared System REMS Requirement
- In October 2018, FDA published revised draft guidance: *Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act*

Encouraging Development of Generic Drugs in Markets with Limited Competition

- List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic (Published in June 2017; updated biannually)
- Addition of patent submission dates to the Orange Book where available (Nov. 2017)

Resources

Who to Contact for Questions Related to Generic Drugs

Brief videos highlighting new features in GDUFA II on FDA.gov:

- GDUFA Overview
- Pre-ANDA Program for Complex Products
- Type II Drug Master Files (DMF) Update
- Performance Goals
- Goals Integration
- Review Status Updates
- Post Complete Response Letter (CRL) Meeting
- Requests for Reconsideration
- Review Classification

Podcasts/Webinars

SBIA Complex Generic Drug Workshop (SBIA)	Regulatory Education for Industry: Complex Generic Drug Product Development Workshop	September 2018
Maryll Toufanian, JD	US Generic Drug Policy: Less Cost, Same Impact	Podcast-Recorded
Howard Chazin, MD	Challenges in Generic Drug Safety & Surveillance	Podcast-Recorded
Xiaohui (Jeff) Jiang, PhD	An Overview of Challenges and Opportunities in the Development of Complex Generic Drug Products	March 6, 2018
Kim Witzmann, MD	Overcoming Barriers to Entry for Complex Generic Oral Inhalation Drug Products	March 15, 2018
Sam Raney, PhD	FDA Champions Research to Make Complex Generic Transdermal Products Available to Patients	April 25, 2018
Liang Zhao, PhD	Pioneering Modeling Methodologies in Generic Drug Development	May 17, 2018

Generic Drug Program

Office of Generic Drugs Mission and Vision

Our Mission

OGD makes high quality, affordable medicines available to the public.

Our Vision

OGD is the world leader in the science and regulation of generic medicines.


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