

ANDA Program Performance Review and Tips

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Generic Drugs Forum 2020 - April 15, 2020

The story behind GDUFA II
performance and
how can you be more successful.

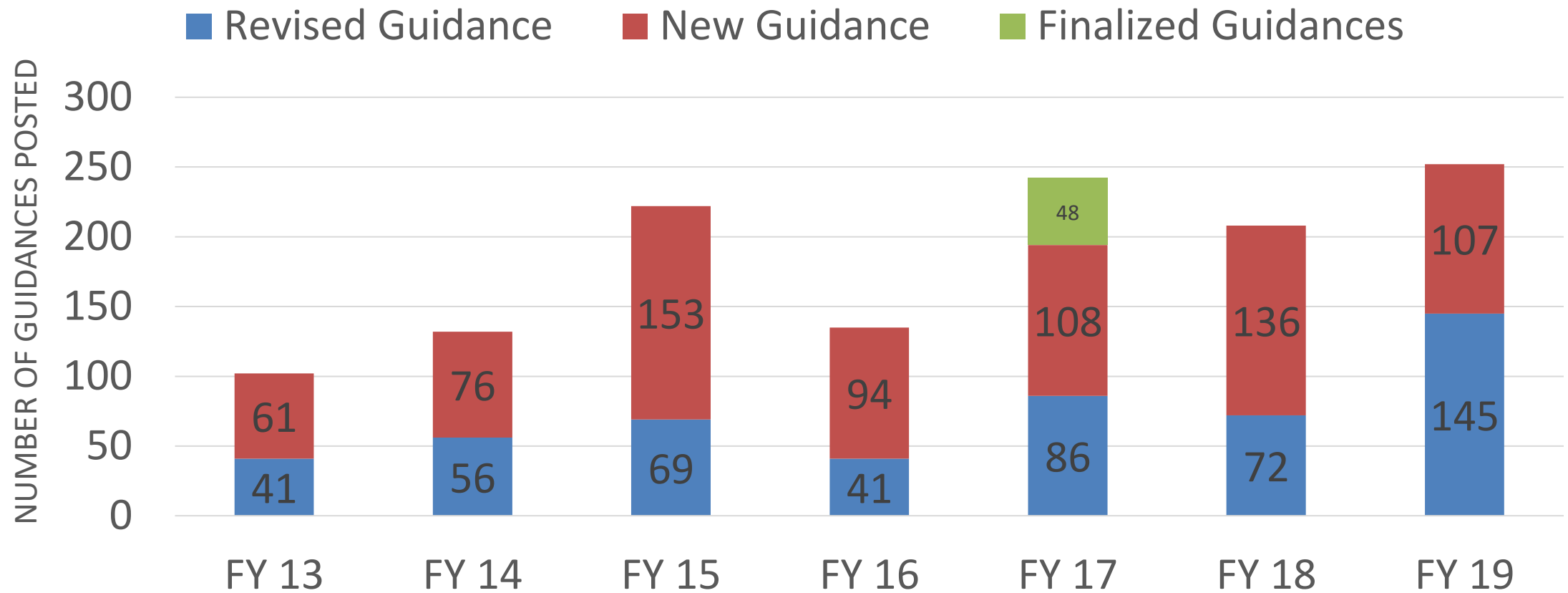
Learning Objectives

- Explain key program metrics
- Provide tips for success
- Provide resources

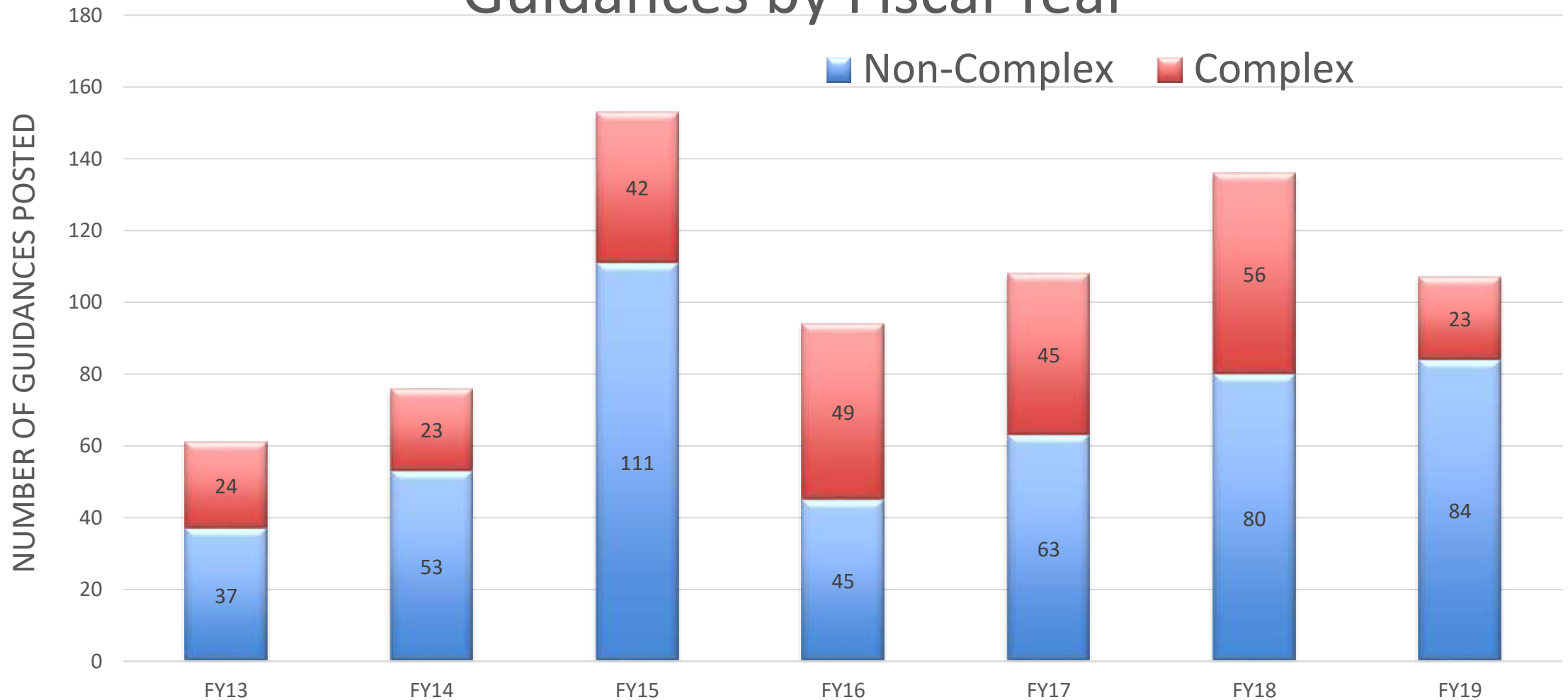
Agenda

- Pre-ANDA Activities
- Filing
- Mid-Cycle Communications
- End of Cycle Communications
- Original Stats
- Supplements
- Challenge Questions
- Concluding Remarks

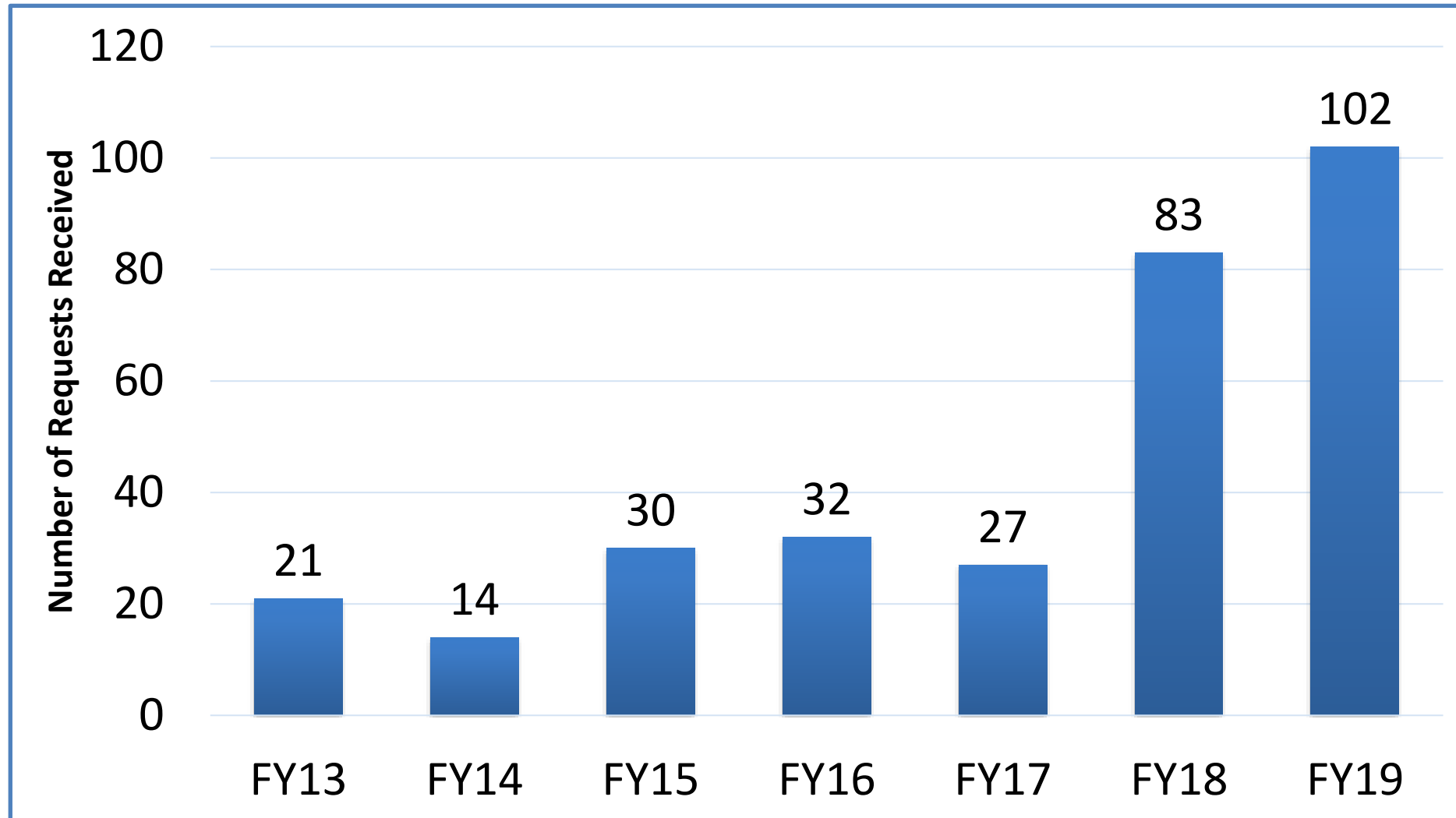
Posted Product-Specific Guidances by Fiscal Year



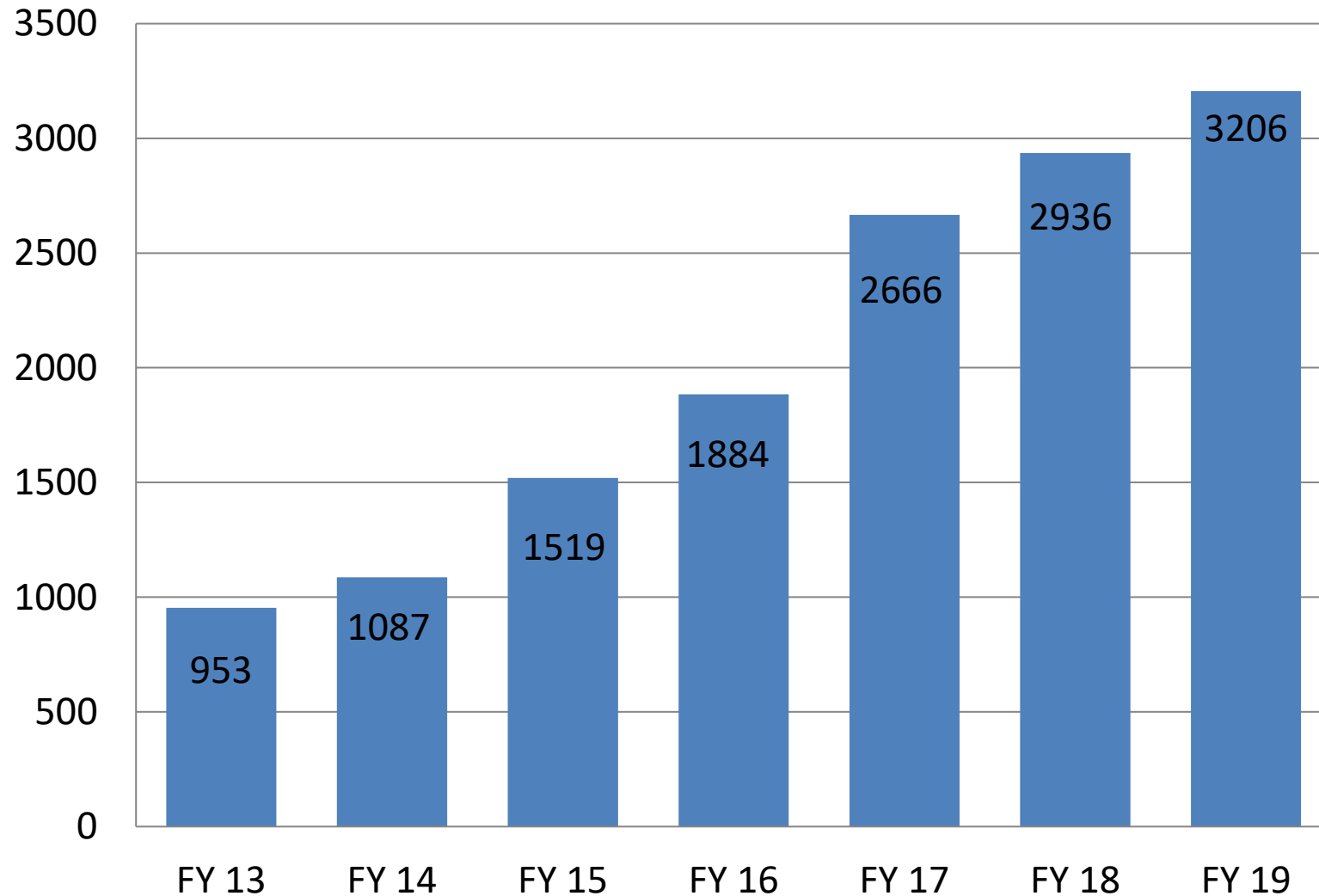
Complex and Non-Complex Product-Specific Guidances by Fiscal Year



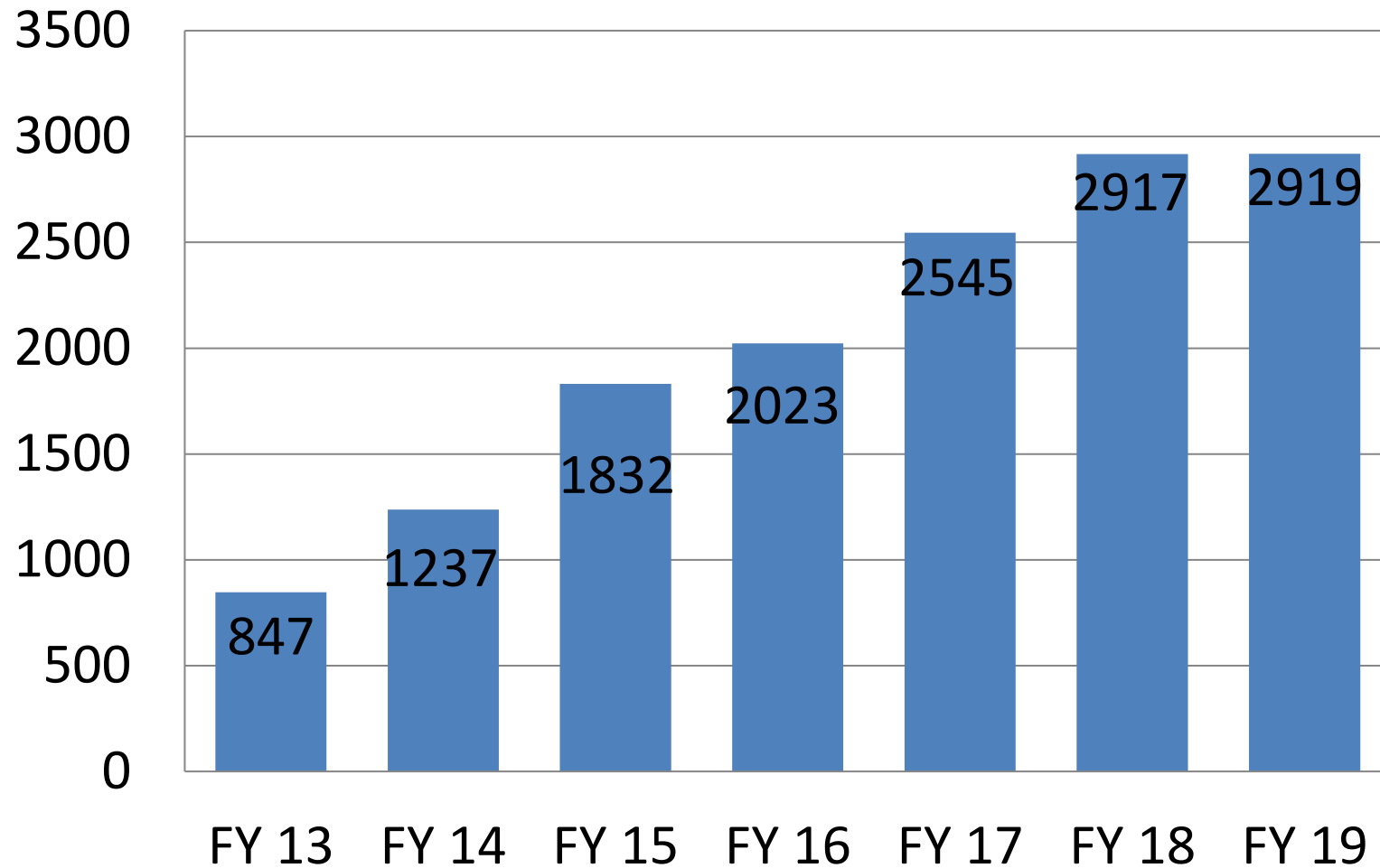
Pre-ANDA Meeting Requests Received



Controlled Correspondence Received



Controlled Correspondence Completed



Top Reasons Controls Were Rejected FY19

- Missing reference and/or copies of previous Controlled Correspondences
- Lacking function and/or hydration states
- Missing RLD (Reference Listed Drug) information
- Multiple disciplines in a single request
- Missing “current” Letter of Authorization (dated within 1 year)
- Missing potential ANDA statement

Controlled Correspondence Tips

- On the top of the cover letter, clearly indicate: Attachments(#)
- Include key information:
 - Relevant RLD
 - RLD application number
 - Proprietary (brand) name
 - Manufacturer
 - Active ingredient
 - Dosage form
 - Strength(s)

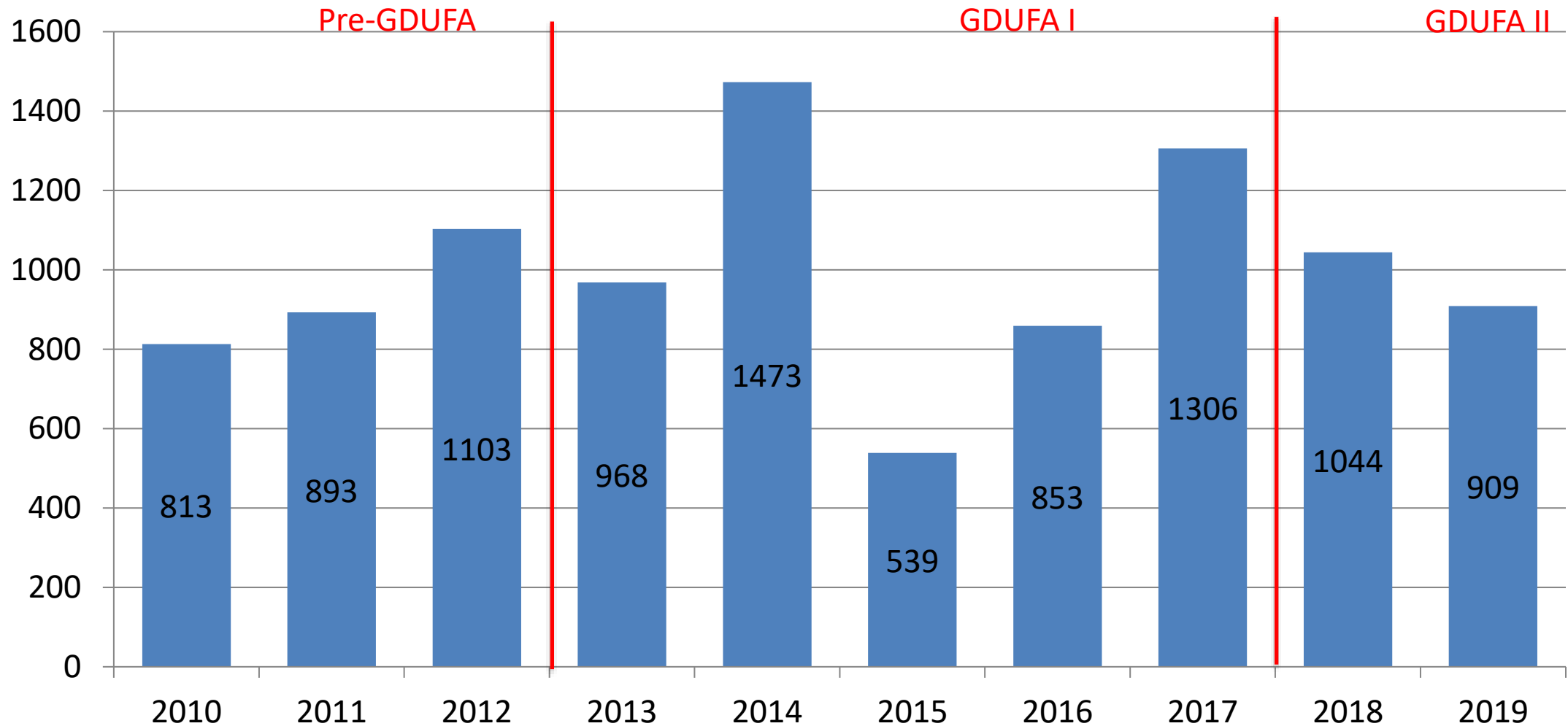
Resources

- [Product-Specific Guidances for Generic Drug Development](#)
- [Upcoming Product-Specific Guidances for Complex Generic Drug Product Development](#)
- [Formal Meetings Between FDA and Applicants of Complex Generic Drug Products Under GDUFA \(Guidance\)](#)
- [Controlled Correspondence Related to Generic Drug Development \(Guidance\)](#)

Agenda

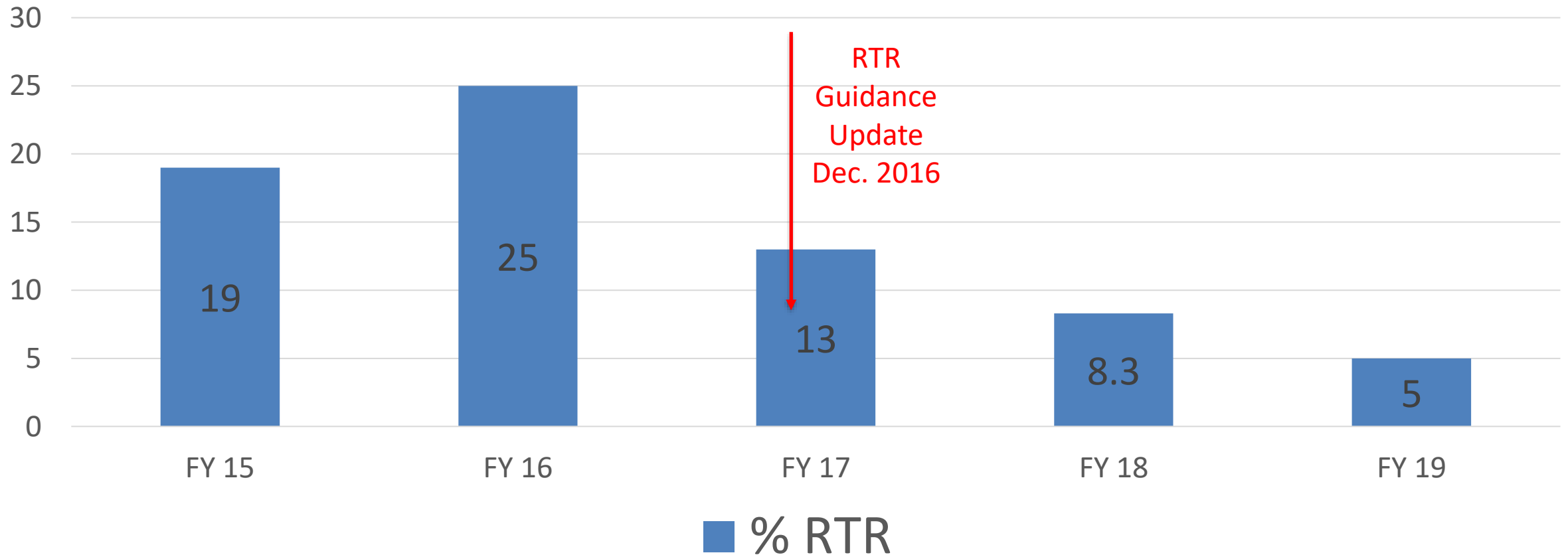
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ANDA Receipts (Originals)



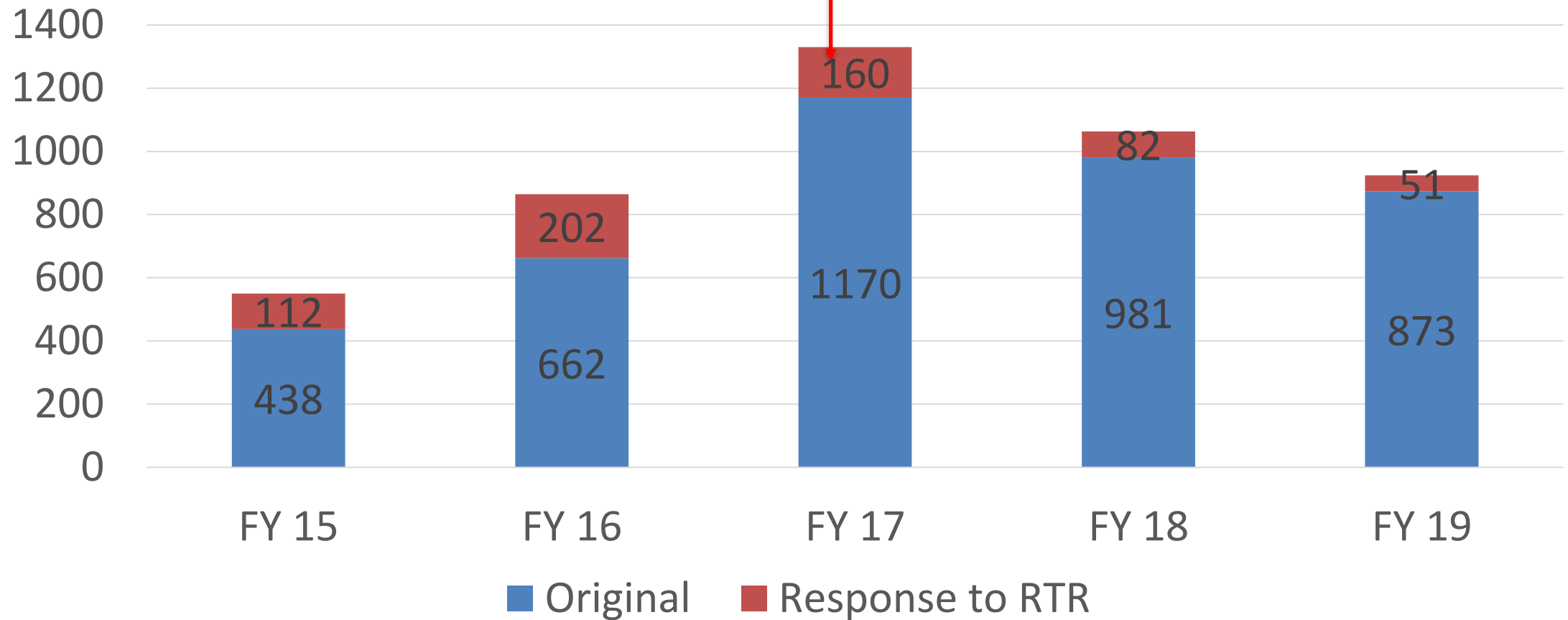
Filing - Refuse to Receive (RTR) Percentage

(Based on cohort year of submission)



RTR
Guidance
Update
Dec. 2016

Impact of Fewer RTRs on Receipts: Totals



Impact of RTRs

- *Not desired state* – we don't want to RTR
 - Pressure to follow procedures, etc.
 - Pressure to be consistent - no exceptions allowed including:
 - Company size or experience
 - Administrative or inadvertent errors

Impact of RTRs (cont.)

- *No value to FDA in RTRs*
 - Additional resources required to issue RTRs
 - Frequent Requests For Reconsideration and Formal Dispute Resolution Requests – very resource intensive
- Potential to delay Approval/Tentative Approval
 - FDA *wants* approvals each month
 - FDA *needs* approvals for drug shortage, 1st generics, etc.

Filing Tips

- Submit a complete application – avoid Refuse to Receive
- *Use the [ANDA Filing checklist](#)*
- Fully complete and sign (and countersign where appropriate) Form FDA 356(h)
- Confirm relevant Type II API Drug Master File (DMF) on Agency's Available for Reference List prior to submitting an ANDA
- Respond completely and timely to Information Requests (IRs)
- Cite issue in IR response

Filing Tips (cont.)

- When correcting communicated electronic Common Technical Document (eCTD) deficiencies:
 - Check all documents for the identified deficiencies
 - Correct where needed
 - Do not duplicate information in the original submission
 - Use correct operation attribute (delete/replace)
 - Contact CDER ESUB at esub@fda.hhs.gov to resolve the matter within the prescribed timeframe
- Place information in proper sections of ANDA hierarchy

Submission Tips

- *Invest in a Quality Application!*
 - Saves you time
 - Saves you money
 - Filing fees
 - Delayed market entry

Submission Tips (cont.)

- Use clear cover letters
 - Type of submission
 - Identify prioritization (originals *and amendments*) and justify
 - Help identify potential consults
 - Help direct your submission to appropriate review groups

Submission Tips (cont.)

- When Referencing a Pre-submission Facility Correspondence (PFC)
 - Submit complete and clear PFC and subsequent ANDA
 - Keep PFC and subsequent ANDA in alignment
 - Clearly note in PFC and subsequent ANDA the priority request and justify it
 - Clearly note in ANDA if part of Pre-ANDA Program

Submission Tips (cont.)

- Think about the assessor
 - Do you want assessor searching for the data or evaluating the data?
 - Consider what assessor will be looking for and provide it
 - Build a reputation for quality submissions
 - Does a sloppy application convey a quality development program?

Submission Tips (cont.)

- Present the data
 - Assessors like to analyze data
 - Ensure all data are completely presented
 - Use clear labels and figures
 - Make data easy to read and compare
 - Make sure data supports the story of your application
 - Use data to show that you know the product

Submission Tips (cont.)

- Referencing communications with the Agency
 - Fully cite Suitability Petition or Citizen Petition and the appropriate Docket Number
 - If you are citing a Controlled Correspondence, include the question and the response in your application
 - Similar for meetings or t-cons with Agency

** Show the value for today!*

Submission Tips (cont.)

- Deviations from guidances
 - Clearly note you are deviating
 - Provide rationale
 - Provide supporting data

Submission Tips (cont.)

- “Say what you do. Do what you say. Prove it. Improve it.”
- Know your product
- Capture that knowledge in the application
- Meet the application criteria
- Comply with requests
- Completely address deficiencies
- ***Repeat the above for contractors***

Submission Tips (cont.)

- Contractors
 - Use responsible contractors (DMFs, etc.)
 - Communicate with contractors (both ways)
 - Know and list all facilities (Manufacturing, Bio, Clinical)
 - *25% of ANDAs referenced DMFs with hidden facilities!*
 - Triggers an amendment from applicant
 - Amendments can impact goal dates

Resources



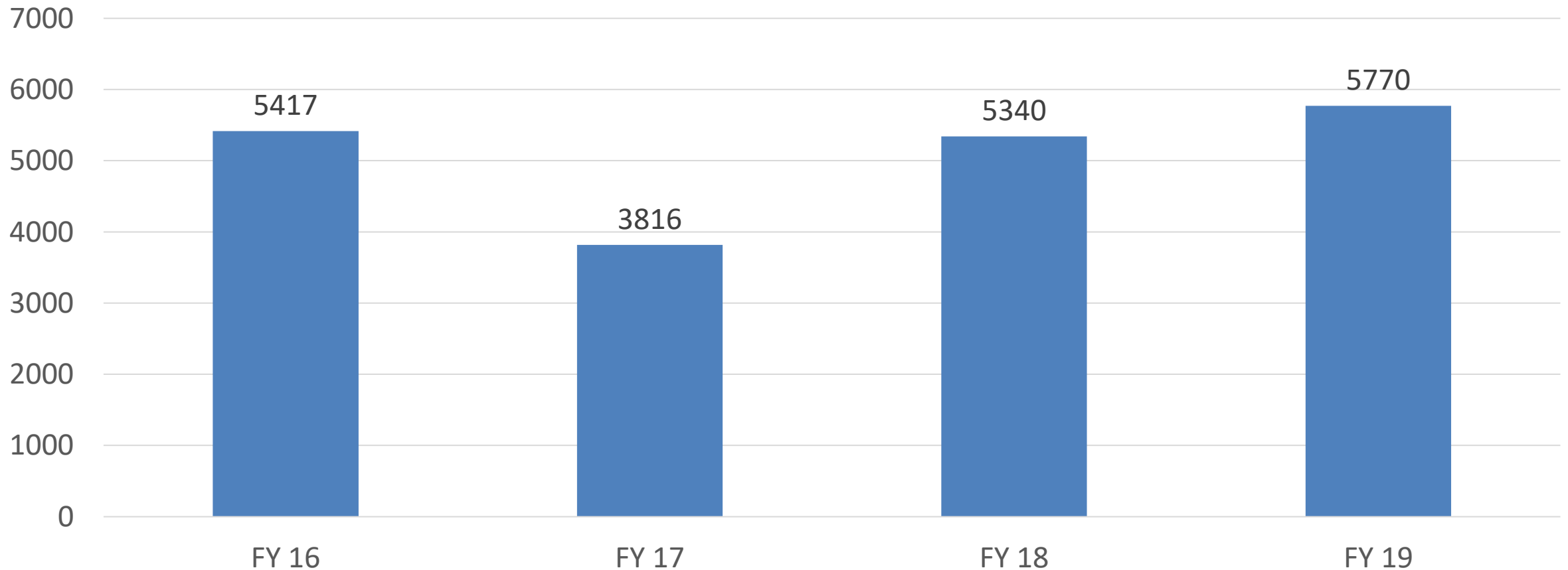
- [ANDAs: Pre-Submission Facility Correspondence Associated with Priority Submissions \(Guidance\)](#)
- [Prioritization of the Review of Original ANDAs, Amendments, and Supplements \(MAPP 5240.3\)](#)
- [ANDA Submissions — Content and Format of Abbreviated New Drug Applications \(Guidance\)](#)
- [ANDA Submissions – Refuse-to-Receive Standards \(Guidance\)](#)
- [Communicating Certain Deficiencies Identified During Filing Review of ANDAs \(MAPP 5220.3\)](#)
- [Filing Review of Abbreviated New Drug Applications \(MAPP 5200.14\)](#)
- [Identification of Manufacturing Establishments...\(Guidance\)](#)

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- Pre-ANDA Activities
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ECDs/IRs/DRLs Issued (originals)

Easily Correctable Deficiencies (ECDs)/Information Requests (IRs)/Discipline Review Letters (DRLs)



Mid-Cycle Tips

- Learn from your deficiencies
- Provide complete and timely responses
- Goal dates are important to FDA too
 - *IR/DRL response delays or questions – start with discipline PM (RBPM for OPQ/Quality)*
- No response to IR or DRL triggers a CRL

Mid-Review Cycle Meetings Tips

- Send the RPM a timeline outlining anticipated responses to any IRs or DRLs pending you/applicant
- *Send the RPM any questions a couple weeks in advance of the meeting* – there is no obligation to respond, but when the questions are appropriate and timely, team will make a good faith effort to address them

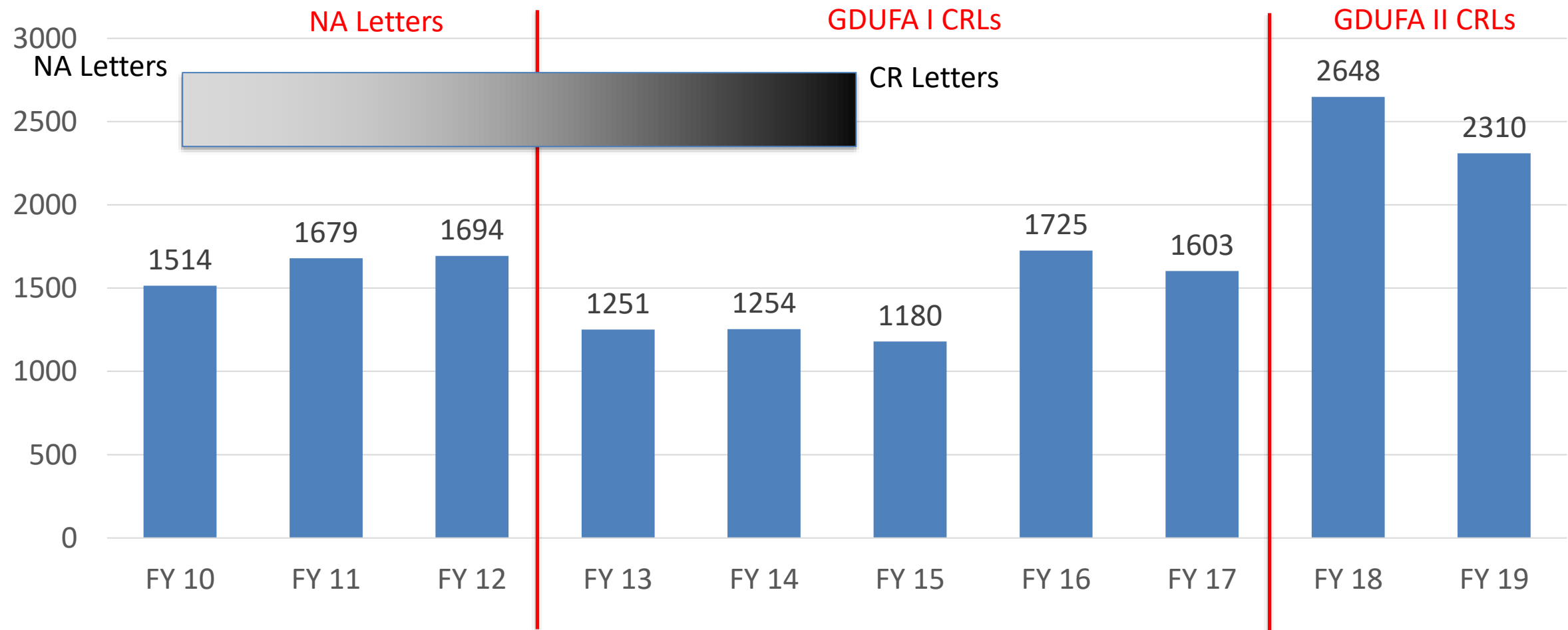
Resources

- [Information Requests and Discipline Review Letters Under GDUFA \(Guidance\)](#)

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Complete Response Letters



Complete Response Tips

- Learn from your deficiencies
- Don't provide extraneous information
- Be accurate
- Be consistent the with the story of your ANDA
- Be timely – help maintain momentum

Use these tips to close out the cycle with an Approval!

Complete Response Tips (cont.)

- *Consider the timing of changes*
 - Unsolicited from applicant
 - Unsolicited and solicited from DMF holder
- *Watch for external changes (RLD, USP, etc.)*
- TA to AP conversion **only** requests should be submitted 3 months prior to AP date

Resources

- ANDA questions during the review process— start with your *Regulatory Project Manager (RPM)*
 - If you cannot reach the RPM, contact the RPM Team Leader then Supervisor
- Contact the RPM, not the discipline unless specifically requested
- RPM cannot rescue ANDAs
- Provide ANDA number when communicating with RPM

Resources (cont.)

- Status Calls with the RPM
 - *Value Added*
 - Mid-cycle date missed (should receive warning from the RPM)
 - No receipt of an IR/DRL late in the 1st cycle
 - No receipt of an acknowledgement of an Amendment
 - No receipt a Post-CRL T-con schedule date > 14 days
 - Periodically as the GDUFA goal approaches
 - Goal date missed (should receive warning from the RPM)
 - Change in applicant contact within your company

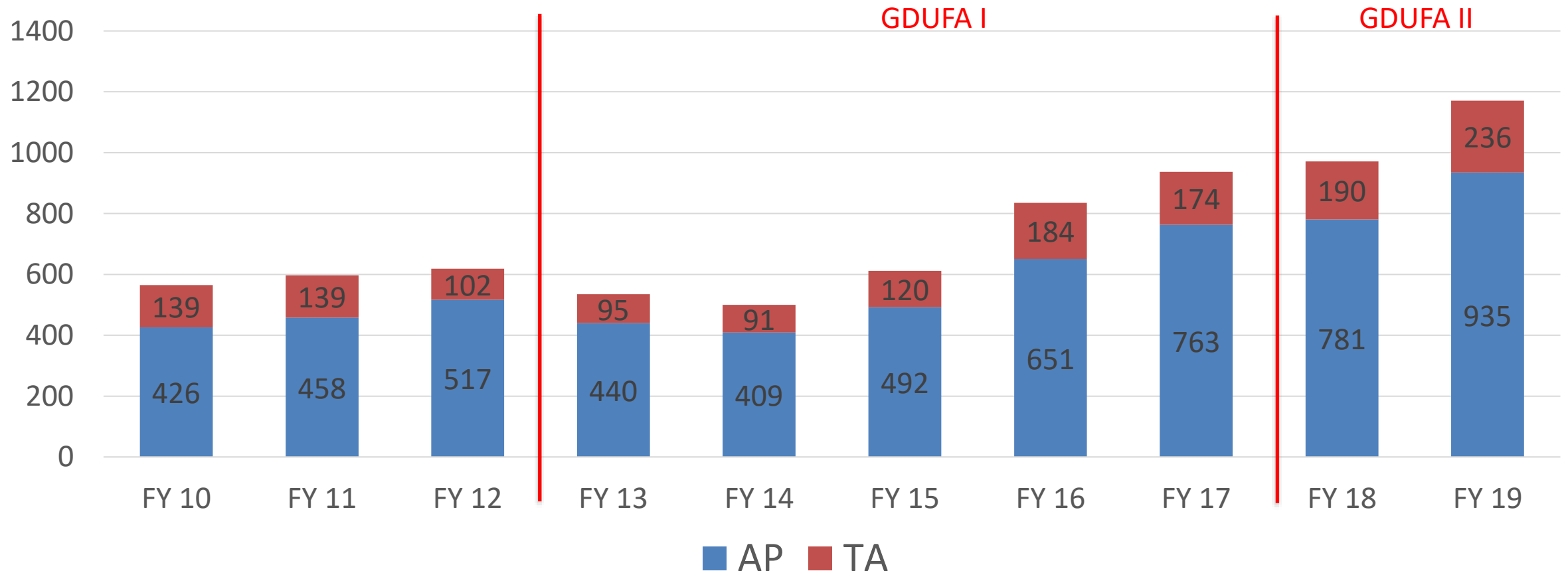
Resources (cont.)

- Status Calls with the RPM (cont.)
 - *Limited value*
 - Prior to mid-cycle date
 - Within two weeks of last status call > 30 days from goal date
 - Within one week of last status call < 30 days from goal date

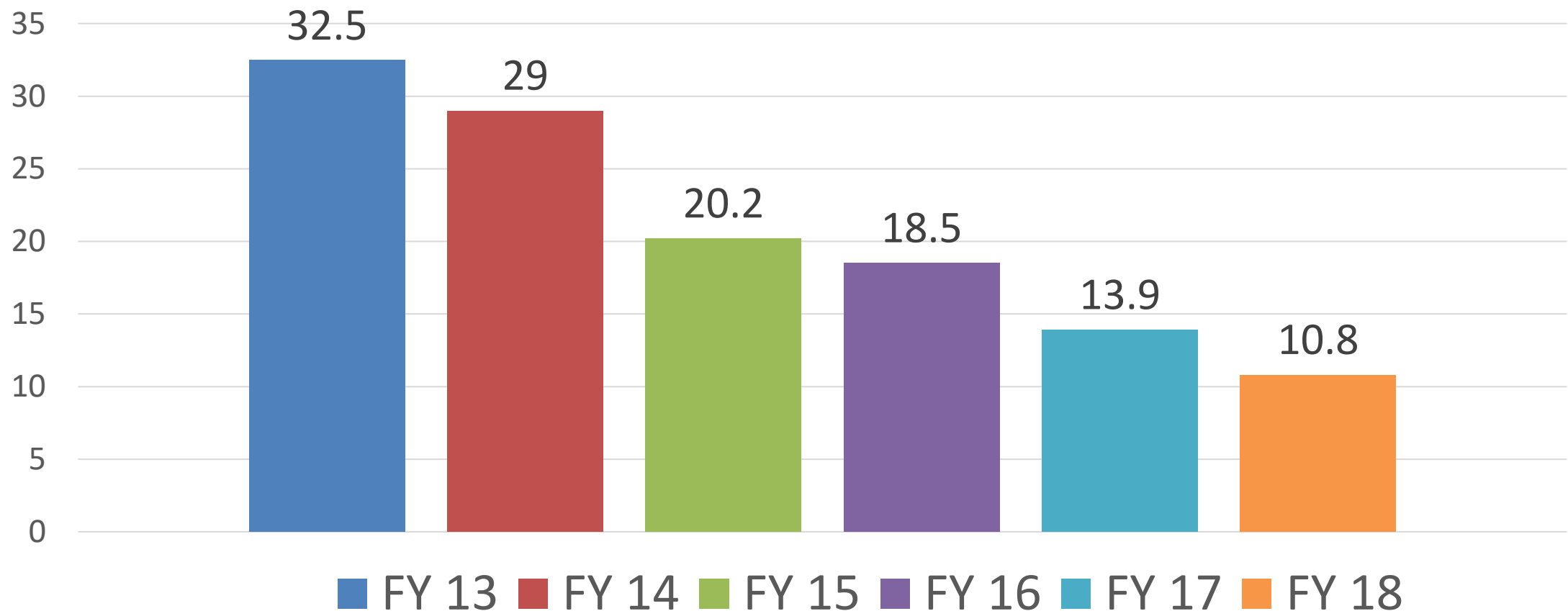
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Approval and Tentative Approval Totals



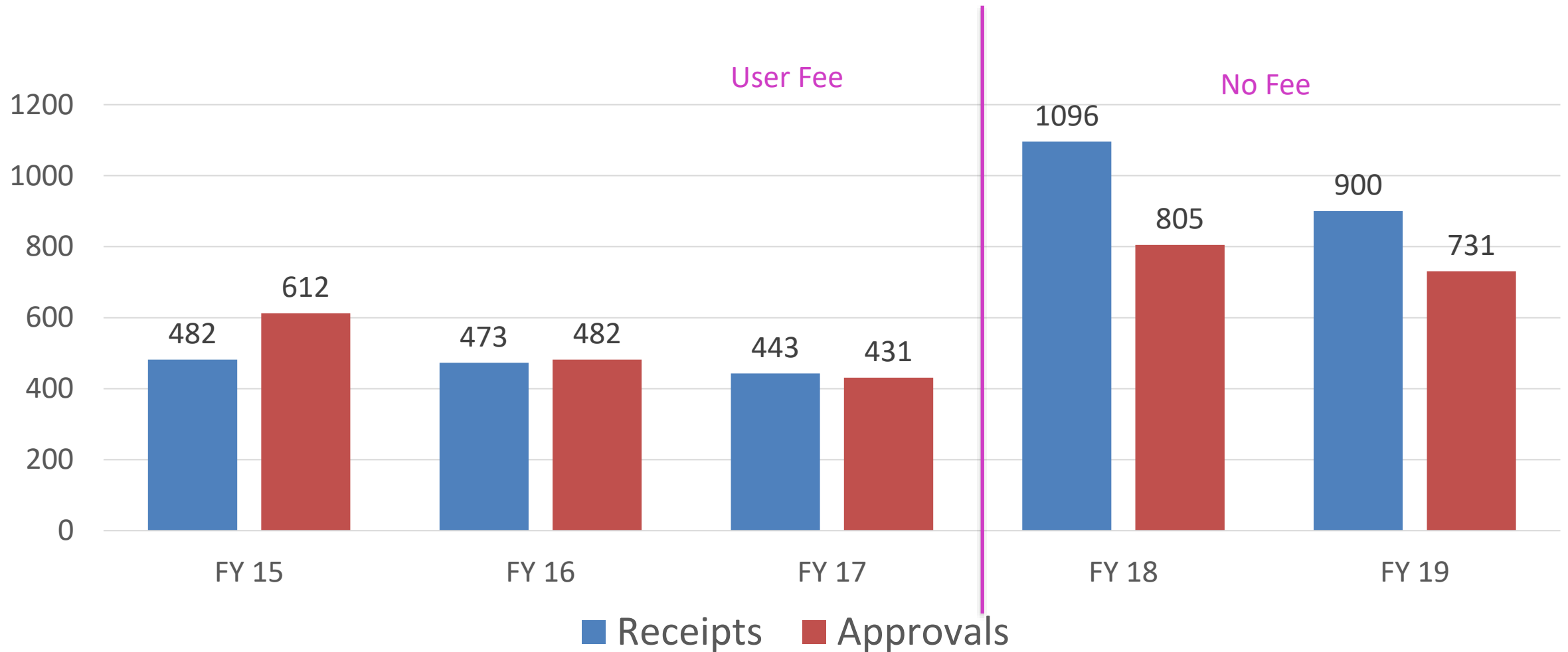
ANDA Median Approval Time: Fastest 25% of Cohort of Receipt Over GDUFA Era



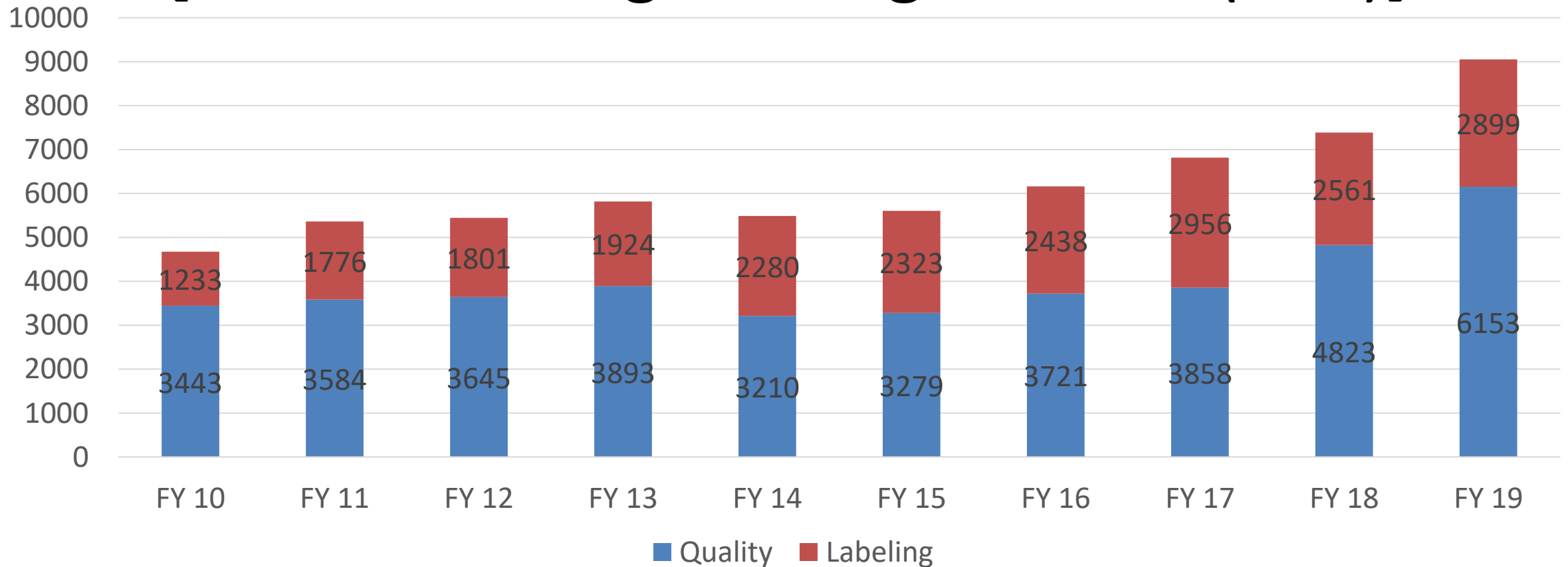
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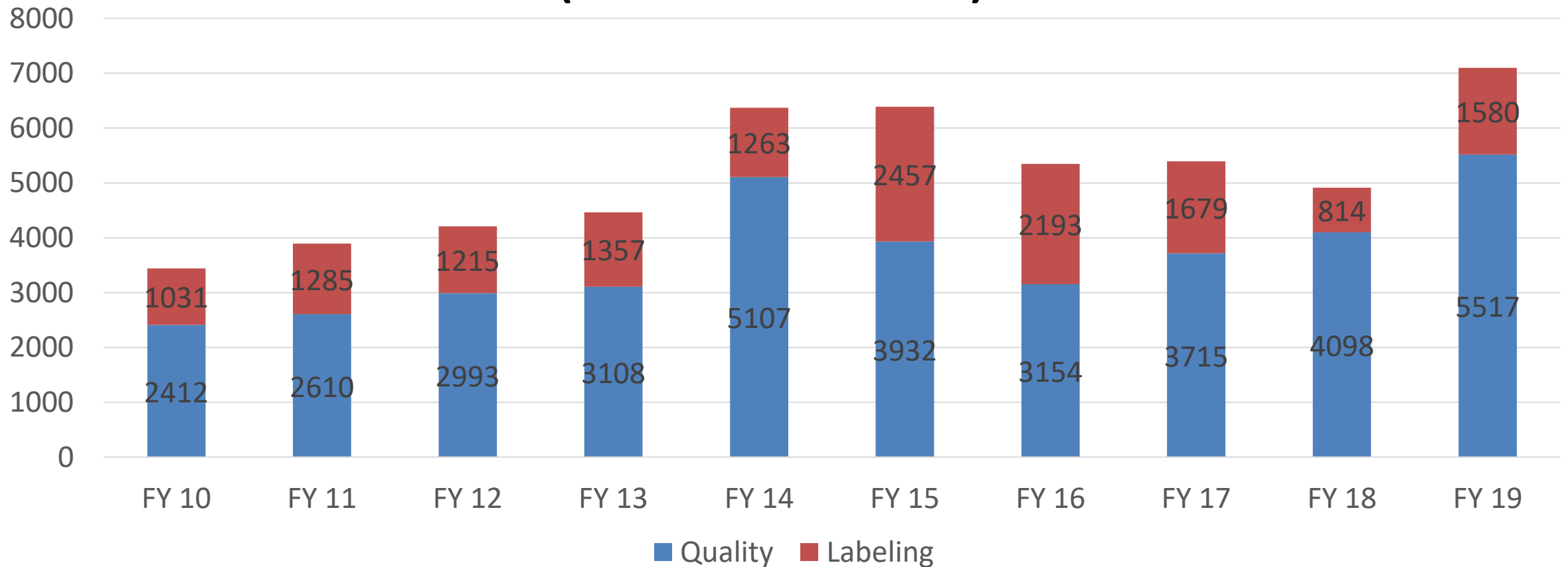
Prior Approval Supplements (PAS) Receipts and Approvals



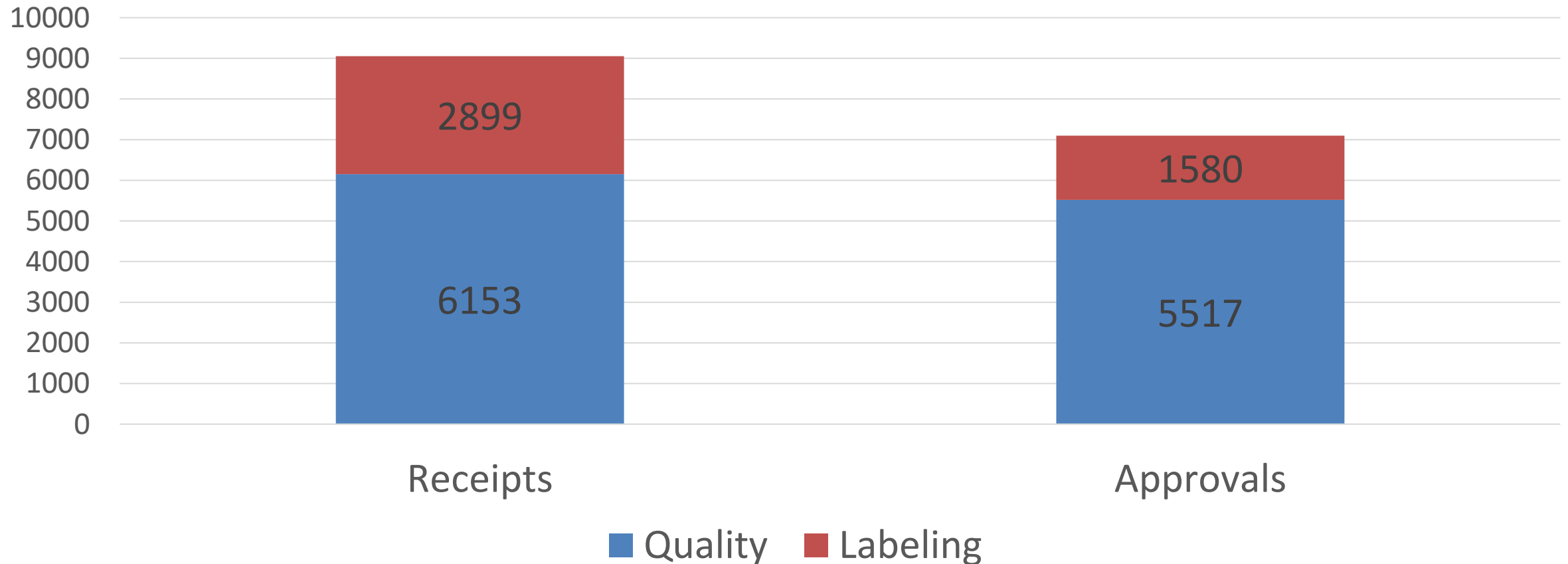
Quality and Labeling Supplements Received 2019 [PAS and Changes Being Effectuated (CBE)]



Quality and Labeling Supplements Approved 2019 (PAS and CBE)



FY 19 Supplement Receipts vs APs (PAS and CBE)



Supplement Tips

- Does the story of your ANDA end with AP?
 - No!
- Does the quality of your ANDA submissions end with AP?
 - No!
- *Carefully assess the nature of the change before determining which type of reporting mechanism is appropriate*
- Provide the appropriate references to data in original application

How Seriously Does FDA Treat the Goals?

- *Very!*
 - Reporting built into GDUFA II program
 - Annual reporting to Congress – explanations for misses
 - The Government Accountability Office (GAO) – expected to audit

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Challenge Question #1

Does FDA want to Refuse to Receive Applications?

Yes

No

Challenge Question #2

Does the story of your application end with approval?

Yes

No

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Concluding Remarks

- The ANDA program is in great shape!
 - Pre-submission communications are increasing
 - Filing acceptance rates are increasing
 - Within-cycle communications from FDA are increasing
 - FDA is exceeding key GDUFA II goals
 - Assessment time with FDA is dropping
 - Approval times for new applications are dropping
- It is a good time to submit an ANDA!

