Office of Generic Drugs (OGD) Update on GDUFA Implementation

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CDER Small Business & Industry Assistance (SBIA)
Generic Drugs Forum (GDF) 2016
April 13, 2016

OUTLINE

1. Opening Comments
2. GDUFA Update
3. Output & Productivity
4. Update on Pre-Year 3 cohort

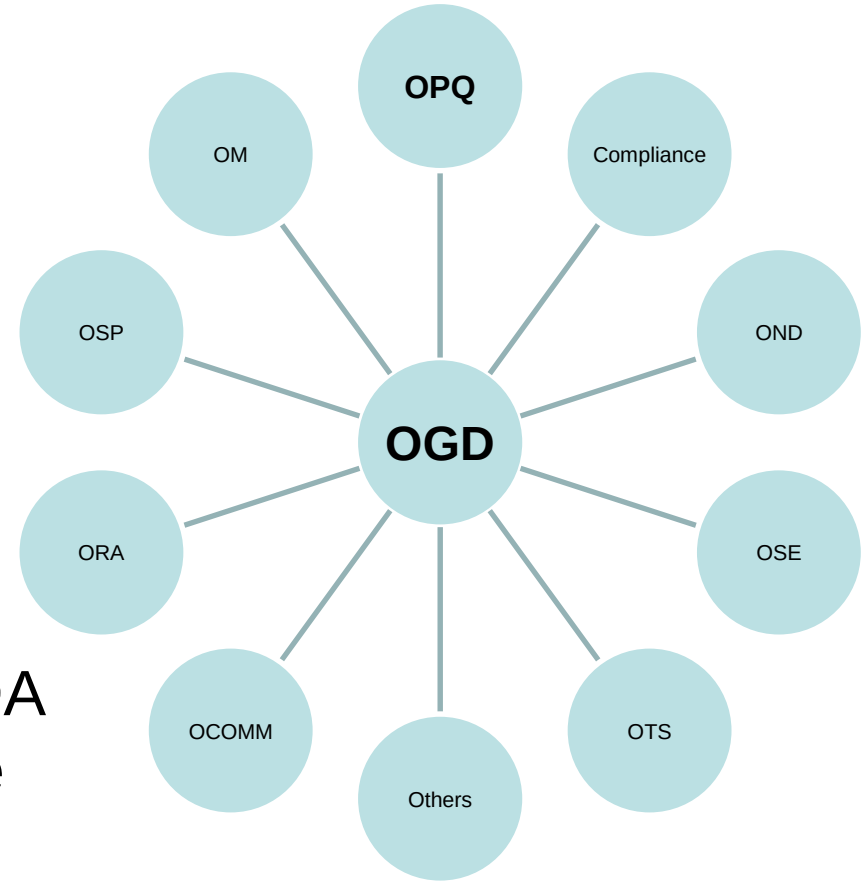
OUTLINE

1. **Opening Comments**
2. GDUFA Update
3. Output & Productivity
4. Update on Pre-Year 3 cohort

GENERIC DRUG PROGRAM

- Not just OGD
- All of CDER
- Other FDA units:
  - ORA
  - Office of the Commissioner
  - OCC
  - CDRH, CBER

- OGD is the interface for ANDA applicants to interact with the Generic Drug Program



GDUFA IMPLEMENTATION

- Agency is meeting ALL of its obligations under the GDUFA commitment letter
- We are going above and beyond the commitments
- Building a modern, 21st Century generic drug program
- Resulting in significant and sustained increase in communications, actions & approvals

QTR 1 & 2 FY2016

(October 2015 to March 2016)

- Approvals – 348
- Tentative Approvals (TA) - 92
- Complete Responses (CR) – 690
  (with and without inspection)

- December 2015 – highest number of approvals/TA in one month EVER at 99
- March 2016 – 2nd highest at 70

- In CY2015 – broke 700 AP + TA
  HIGHEST NUMBER EVER

*Numbers are based on current data and will be further scrubbed for formal reporting purposes
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm375079.htm

OUTLINE

1. Opening Comments
2. **GDUFA Update**
3. Output & Productivity
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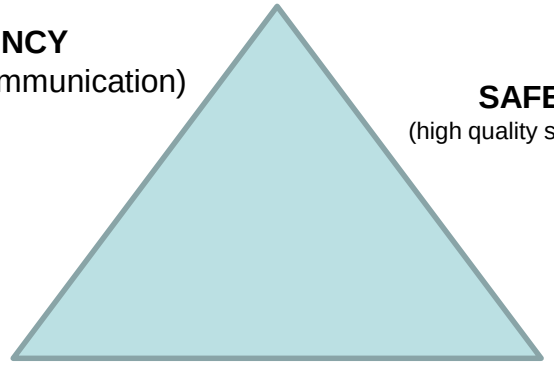
GDUFA MAJOR PROGRAM GOALS

(5 year plan)

1. Metrics
   - Applications
   - GDUFA Backlog
   - cGMP Inspections
2. Efficiency enhancements
3. Regulatory science



GDUFA GOAL DATES

Powerful tool to improve the timeliness and predictability of review

Goals	Review Time	FY2015	FY2016	FY2017
Original ANDA submission	15 months	60%	75%	90%~
Tier 1 first major amendment	10 months	60%	75%	90%
Tier 1 minor amendments (1st-3rd)	3 months*	60%	75%	90%
Tier 1 minor amendments (4th-5th)	6 months*	60%	75%	90%
Tier 2 amendment	12 months	60%	75%	90%
Prior Approval Supplements	6 months*	60%	75%	90%
ANDA teleconference requests	10 business days	200	250	300
Controlled correspondence+	2 months	70%^	70%	90%
ANDAs, amendments and PASs in backlog on Oct 1, 2012	*Act on 90% by end of FY2017*			

Note: Performance goals in the chart means FDA should take a "first action" (as defined above) on a certain percent of applications, etc. within the timeframes listed; it does not mean FDA should approve applications, etc. within such timeframes.
+If no input required from clinical division
***10 months if inspection required**
^4 months
~10 months

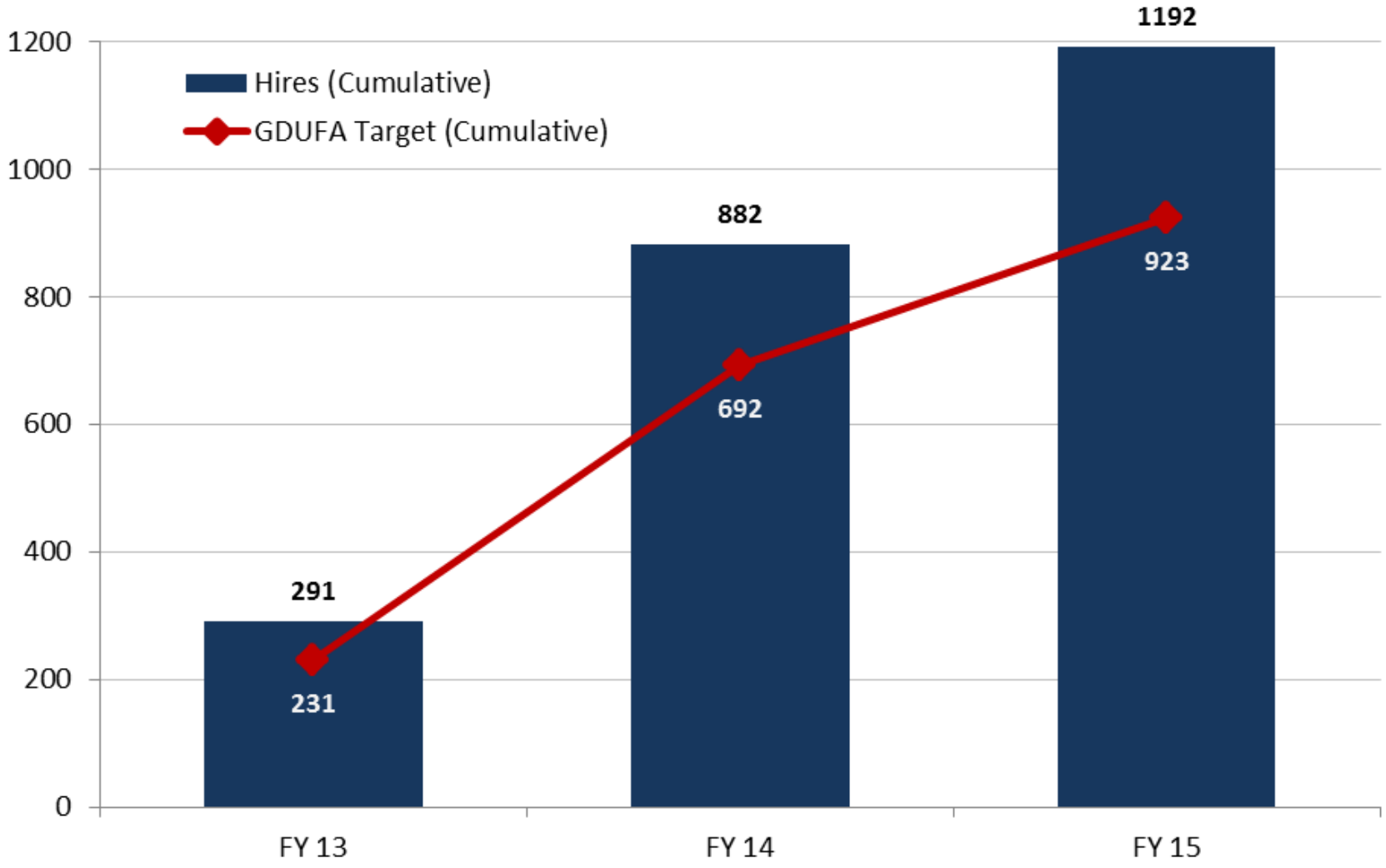
GDUFA IMPLEMENTATION

Build the Machine

- Deep foundational restructuring
- Build infrastructure
- Improve business processes
- Hire and train new staff
- New IT platform
- Improve communications

- All to prepare for Year 3 Goal Dates AND to enable us to hit goal dates

GDUFA Hiring Progress

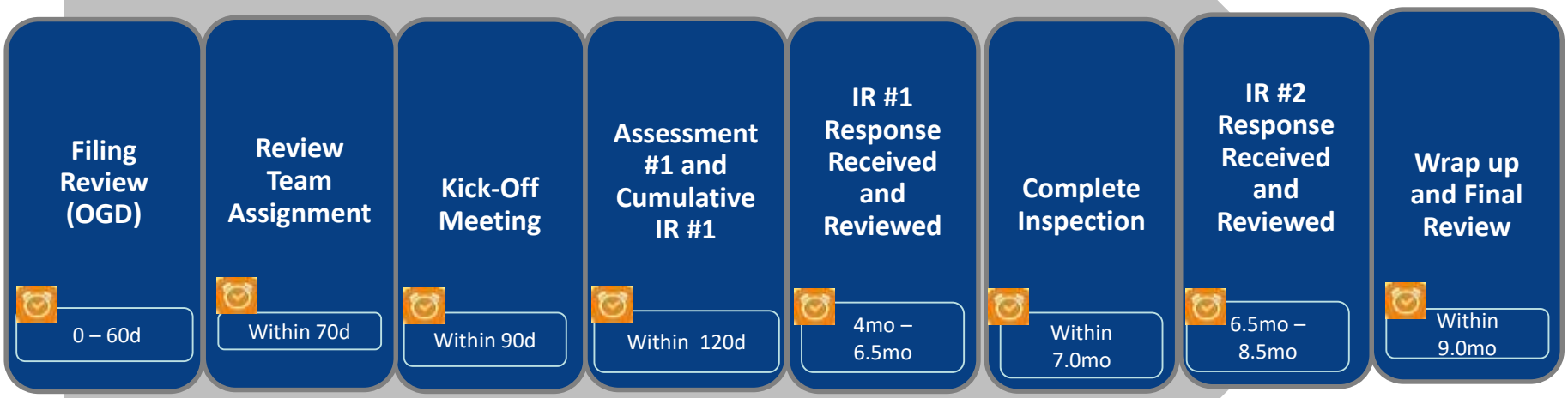


CDER Informatics "Platform"

- Improved communication and increased productivity are the direct result of our improved IT system for the generic drug program
- Provides workload management & review management tools
- Enables prioritization process for 1st generics, PIVs, exclusivity type issues
- OVER **130,000** assignments in new Platform

PREDICTABILITY for INDUSTRY

Proposed example of Year 5 timeline:



OGD & OPQ believe, in working with Industry, by Year 5 the 1st cycle approvability rate for ANDAs can be improved.

This goal is achievable provided that upon first submission, the ANDAs are of high quality and complete to allow for FILING & Scientific Review, i.e. ANDA "approvability."

GDUFA

TRANSFORM THE PROGRAM
and
PERFORM WHILE TRANSFORM

We built the machine…
NOW we are cranking it up!

OUTLINE

1. Opening Comments
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3. **Output & Productivity**
4. Update on Pre-Year 3 cohort

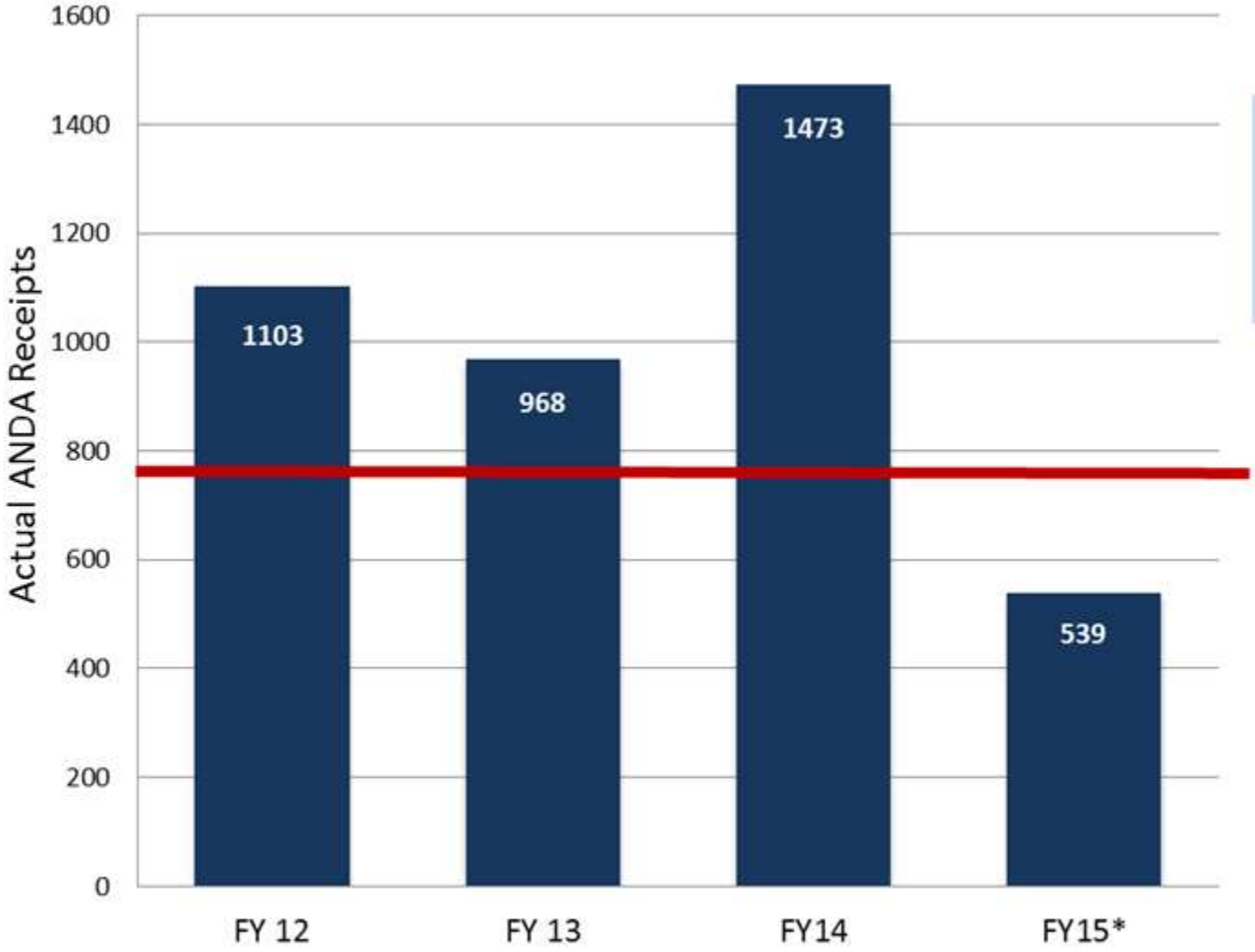
OUTPUT & PRODUCTIVITY

INCOMING from INDUSTRY

OUTPUT from FDA

- GDUFA Backlog
- ANDAs
- PASs
- Filing
- Communication
- Controlled Correspondence
- Guidance

PROJECTED vs ACTUAL ANDA RECEIPTS

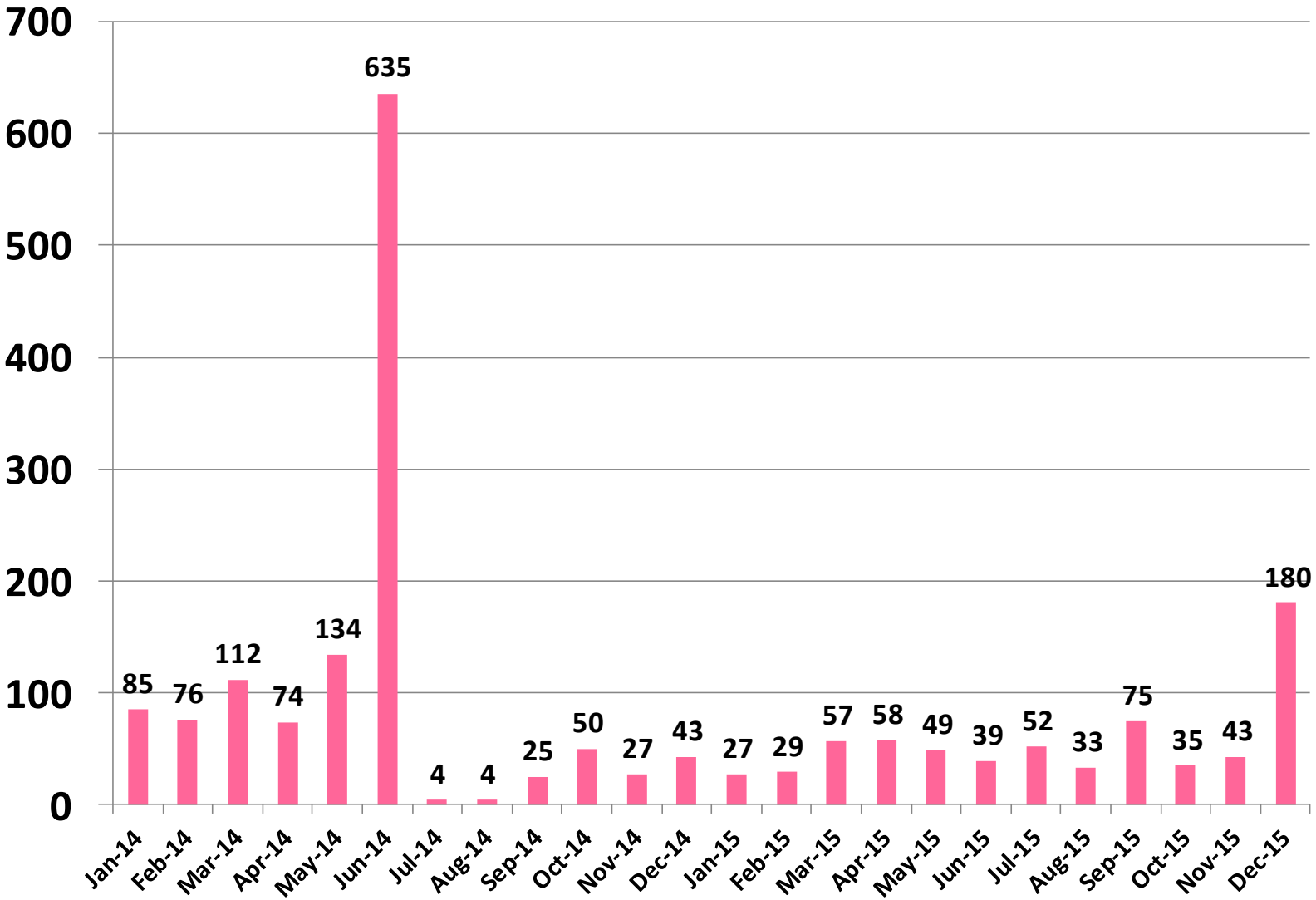


FDA Received Approximately 5.5 Years of Projected ANDA Receipts in 4 years

750 Projected ANDAs per year

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

Monthly ANDA RECEIPTS



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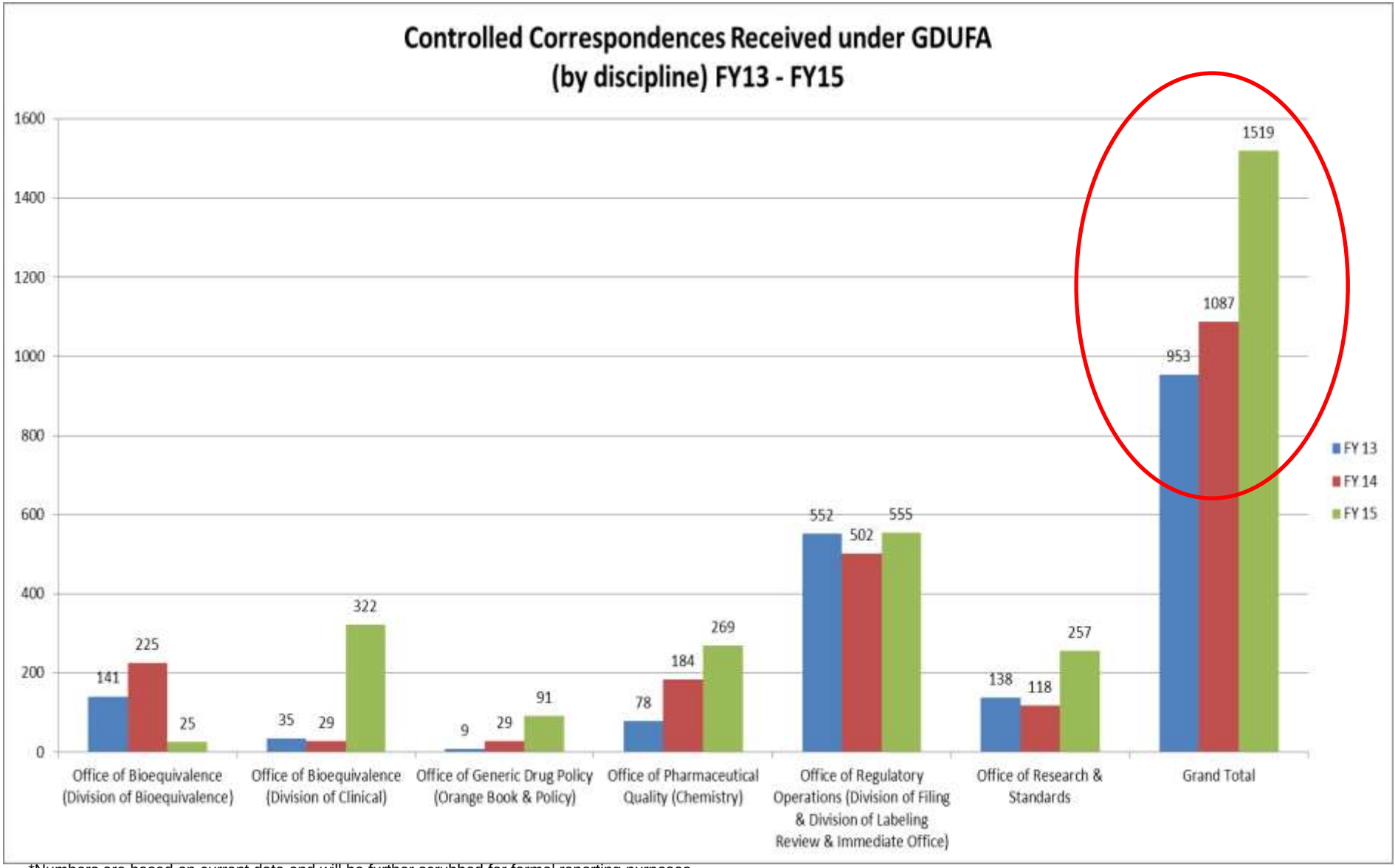
CONTROLLED CORRESPONDENCE RECEIPTS



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OVERALL ACTIONS

PRE-GDUFA | GDUFA

	FY2012	FY2013	FY2014	FY2015*
ANDA approvals	517	440	409	492
Tentative Approval (TA)	102	95	91	120
PAS approvals	275	535	659	624
Complete Response (CR)	84	1251	1254	1007
TOTAL **	978	2321	2413	2243
DMF Completeness Assessment (CA)	0	1699	1706	901

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

** 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)
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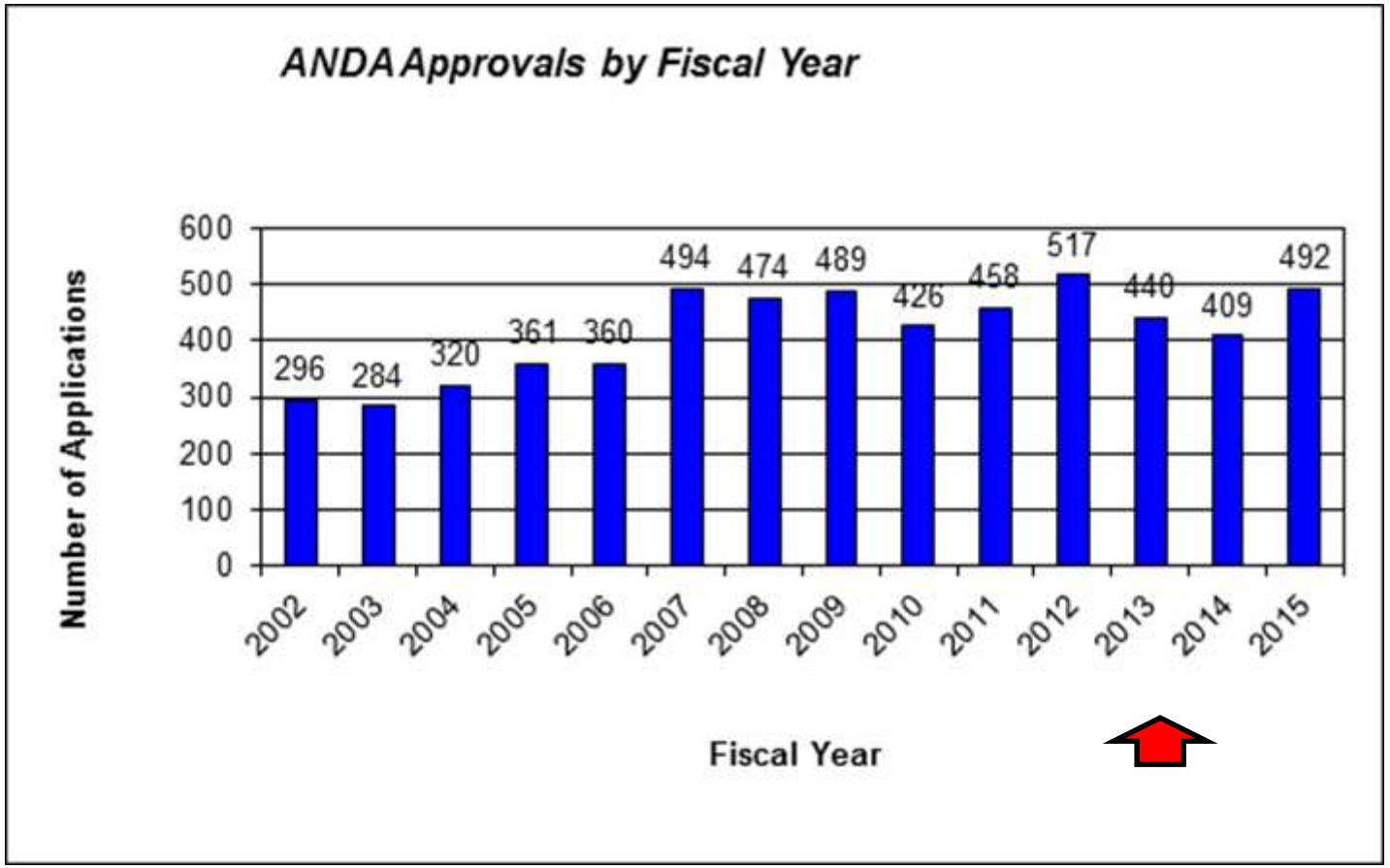
ANDA Approvals

PRODUCTIVITY



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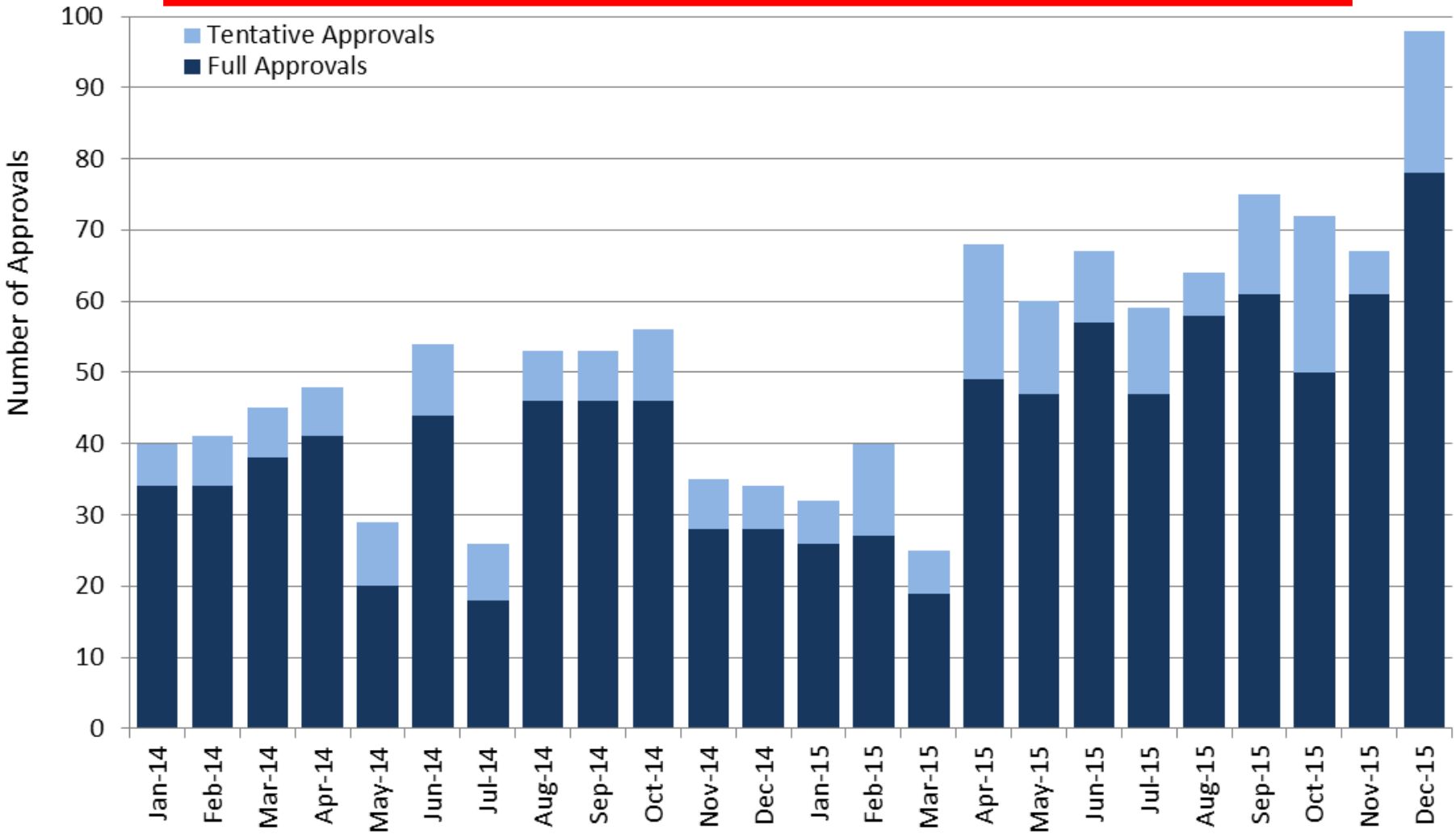
APPROVALS AND TENTATIVE APPROVALS

FY2014, FY2015 & Q1FY2016
(GDUFA YEARS 2, 3, Q1Yr4)



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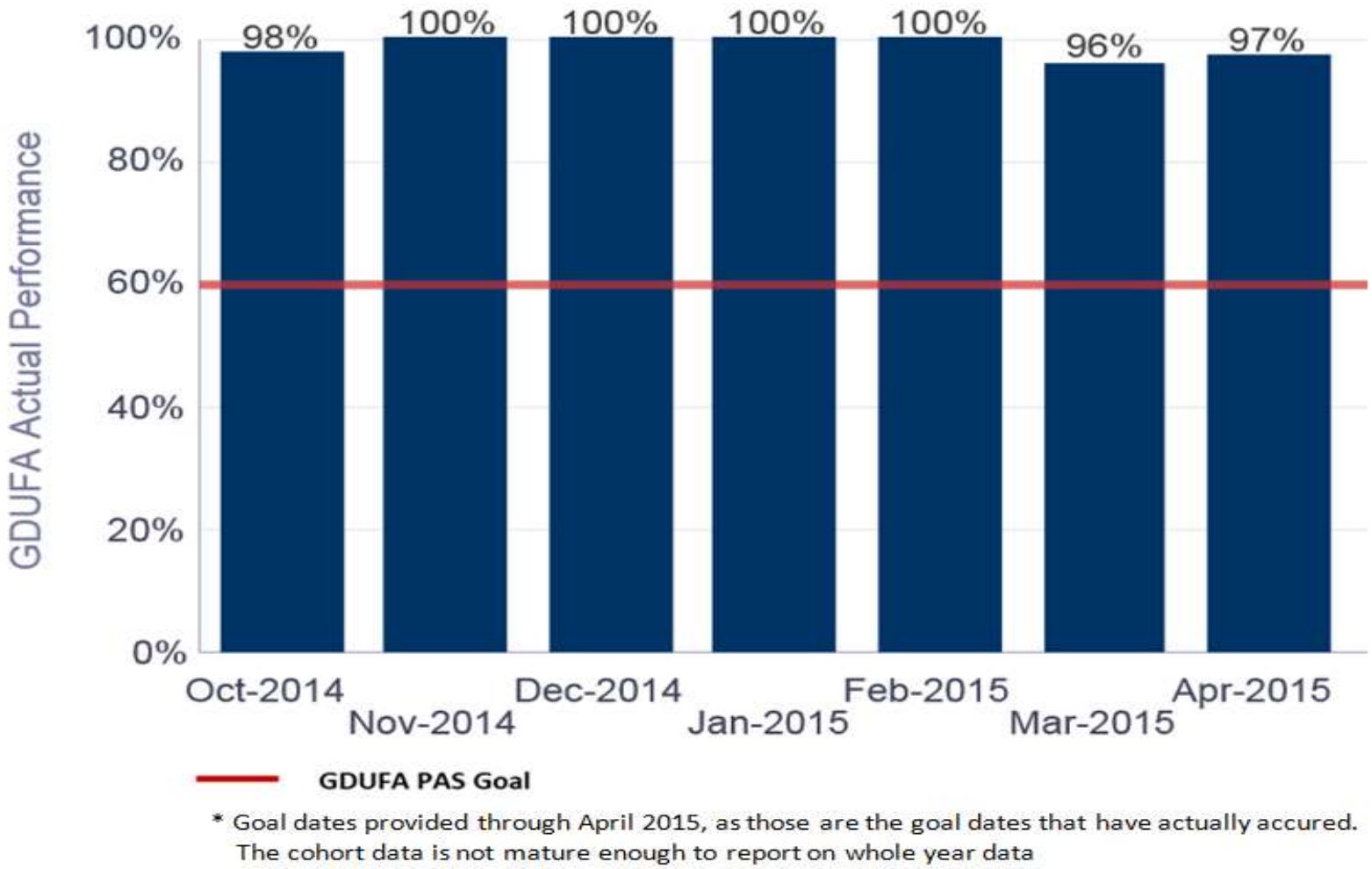
Significant "First Generic" Approvals for 2015

Brand (Generic name)	Indications (Abbreviated)
Abilify® (aripiprazole)	Schizophrenia, Bipolar Disorder
Copaxone ® (glatiramer)	Multiple sclerosis
Enablex® (darifenacin)	Overactive bladder
Fusilev® (levoleucovorin)	Supports cancer treatment
Lotronex® (alosetron)	Irritable bowel syndrome
Integrelin® (eptifibatide)	Heart attack
Norvir ® (ritonavir)	HIV-1 infection
Orap ® (pimozide)	Tourette's Disorder
Transderm Scop® (scopolamine)	Motion sickness
Tygacil® (tigecycline)	Pneumonia, serious infections
Vagifem® (estradiol)	Menopause
Xenazine® (tetrabenazine)	Huntington's Disease
Zyvox® (linezolid)	Pneumonia, serious infections

Prior Approval Supplements (PAS)

Exceeding GDUFA Review Goals*



* Goal dates provided through April 2015, as those are the goal dates that have actually accured. The cohort data is not mature enough to report on whole year data

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GDUFA Backlog Applications with First Action through 12/31/15

Actions	ANDAs	PASs
Number with First Action*	2,414	1,666
Percentage Complete	**84%**	**88%**
Approval	609	959
Tentative Approval	151	4
Complete Response with an Inspection**	1,384	465
Refuse to Receive	69	2
Withdrawn Application	201	236

* Numbers reflect data available at the time of report publication and may change based on refreshed counts in our tracking systems, including application status updates. These numbers are not intended for Congressional reporting purposes.
**Complete Response with an Inspection is a written FDA communication to an applicant usually describing all of the deficiencies that the agency has identified in an application that must be satisfactorily addressed before it can be approved.

GDUFA BACKLOG:
2,866 original ANDAs
1,873 PAS supplements

GDUFA GOAL:
90% get first ACTION by end of GDUFA YR 5 (9/30/2017)

FILING REVIEW

- There is **NO** filing backlog
  - Pre-year 3 applications: Done!
  - Reviewed, filed or RTRed
  - FY 2015 ~1,500 filing reviews completed

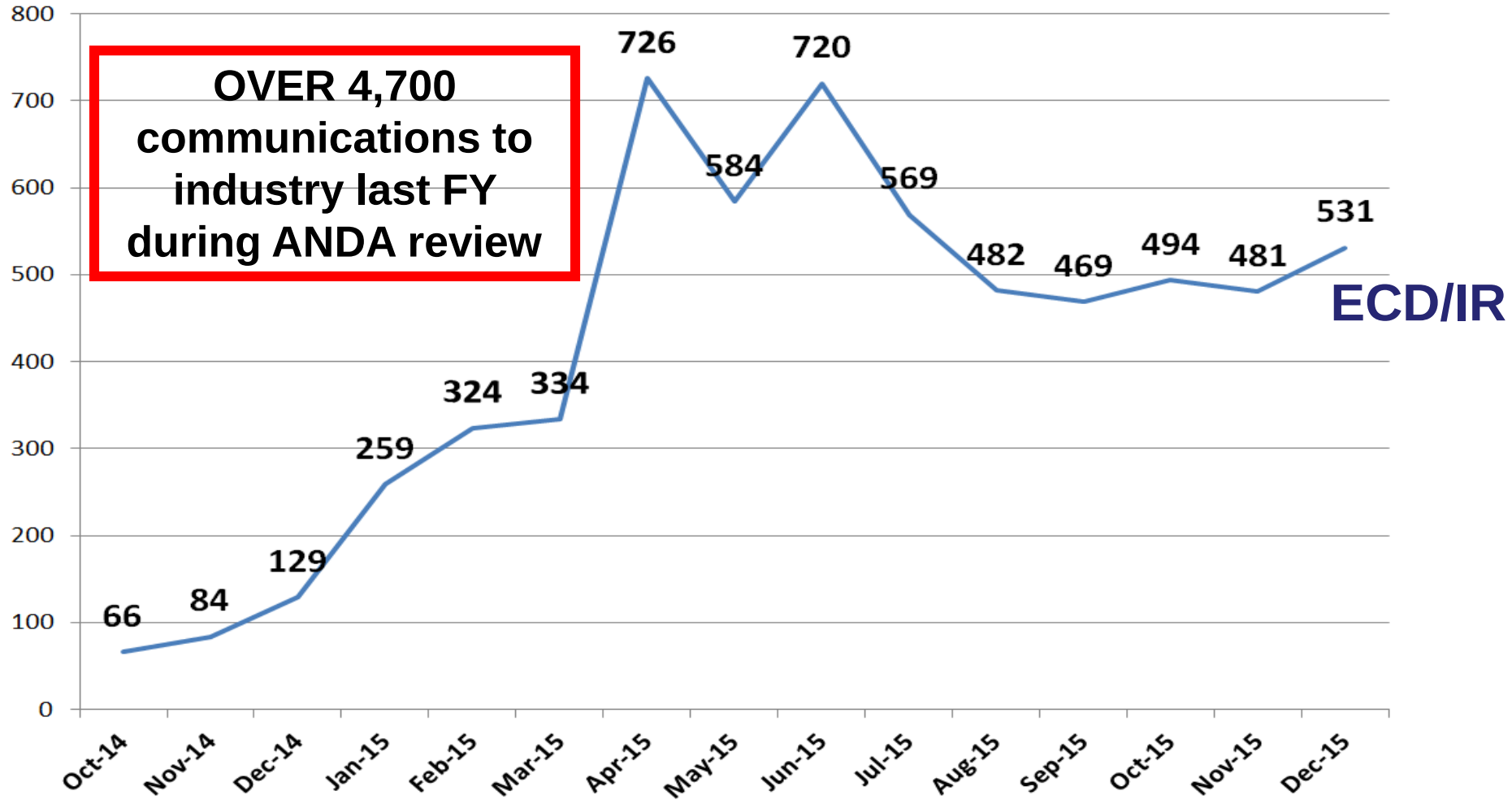
- Filing being done in real time
  - Current: 31 days

FILING

- First step in REVIEW
- Acceptable for FILING means that the application is sufficiently complete to permit substantive review
- It does not mean that the application will be approved
- 1st inning home run vs. winning the ball game

PRODUCTIVITY: COMMUNICATION WITH INDUSTRY

EASILY CORRECTABLE DEFICIENCIES (ECDs) & INFORMATION REQUESTS (IRs)



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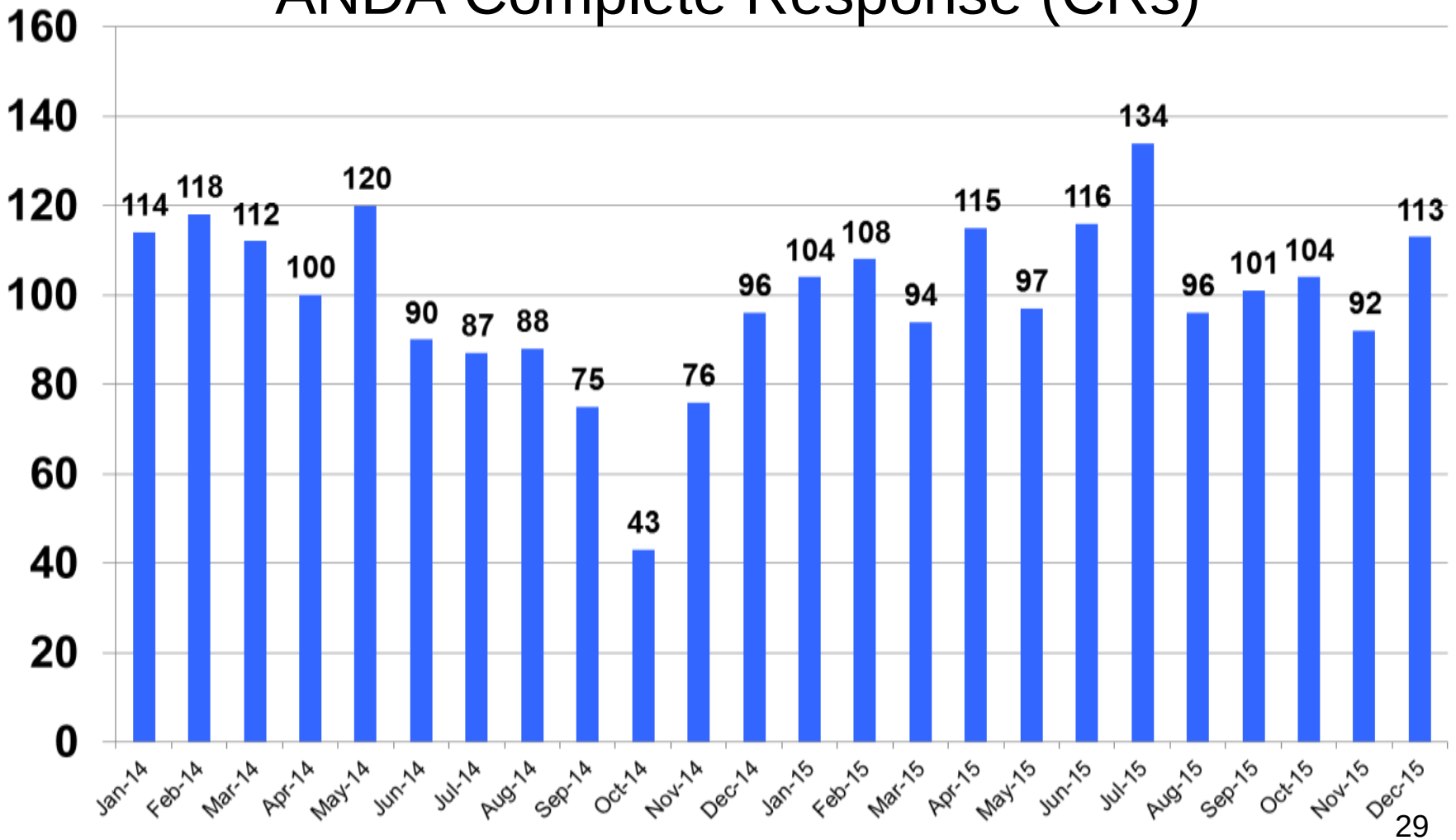
PRODUCTIVITY:

ANDA Complete Response (CRs)



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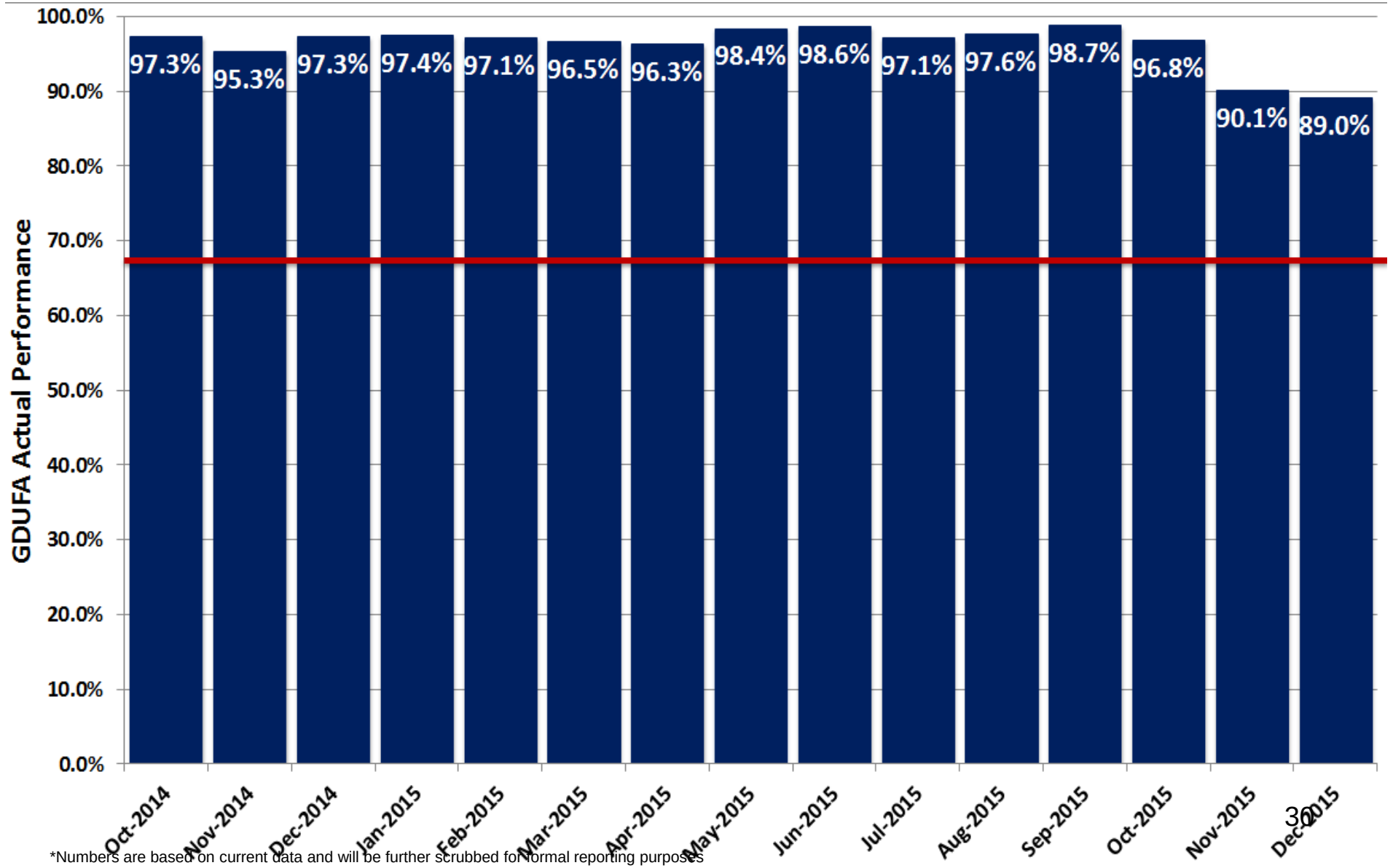
Exceeding Controlled Correspondence Goals



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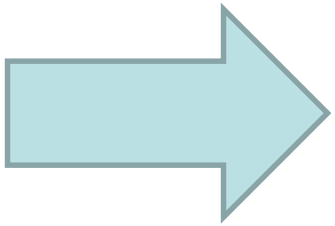
Application "approvability"

Upon first submission, the ANDAs are of high quality and complete to allow for complete and adequate FILING & Scientific Reviews

Completeness:

1. For Filing
2. During Scientific Review



RTR

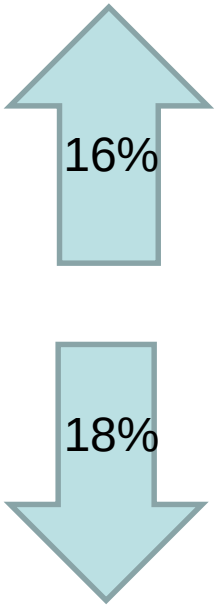
1st cycle approval

Multiple review cycles

FILING – Refuse to Receive (RTR)

(Based on cohort year of submission)

YEAR	# RTR's	% of Cohort
FY2010	146	18%
FY2011	142	16%
FY2012	156	14%
FY2013	193	19%
FY2014	191	13%
FY2015	124	23%



Compared with first years of PDUFA: 10-30% Refuse to File (RTF)

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

Cohort Year 3 APPROVALS

Through 3/31/16 (15 month goal)

Active Ingredient	ANDA Number	Company	Date of Approval
Tretinoin	207955	Spear	08/13/2015
Loperamide*	206548	Aurobindo	12/15/2015
Gabapentin	206402	Alkem	12/23/2015
Sodium Polystyrene	206815	Invatech	2/18/2016
Desoximetasone	208101	Teligent	2/25/2016
Fluticasone	208150	Apotex	2/29/2016
Levonorgestrel	207976	Novast	3/11/2016
Desipramine	208105	Amneal	3/17/2016
Diclofenac	208077	Amneal	3/18/2016

AP issued on or before GDUFA goal date
*Not a first cycle AP

Information available at: Drugs@FDA website:
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

Cohort Year 3 TENTATIVE APPROVALS (TA)

Through 3/31/16 (15 month goal)

Active Ingredient	ANDA Number	Company	Date of Tentative Approval
Diclofenac	208068	Paddock	10/14/2015
Diclofenac	208098	Taro	01/14/2016
Sildenafil*	206401	Ajanta	01/21/2016
Lurasidone	208031	Lupin	01/25/2016
Lurasidone	208037	MSN Labs	01/25/2016
Lurasidone	208066	Sun Pharma	01/25/2016
Risedronate	205280	Orchid	01/29/2016
Lurasidone*	208055	Torrent	02/5/2016
Lurasidone*	208058	Emcure	02/23/16
Aspirin + dipyridamole ER	207944	Par	03/1/2016
Clofarabine	208167	Zydus	03/4/2016
Efavirenz, Emtricitabine, tenofovir	206894	Cipla	03/22/2106

TA issued on or before GDUFA goal date

*Not a first cycle TA

Information available at: Drugs@FDA website: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

ANDA "Approvability"

(Cohort Year 3: January to March 2016, n=119)

- **14% first cycle approval rate**
- **63% complete response**
  - **CR leads to subsequent or multiple review cycles**
- **>95% met GDUFA goals**

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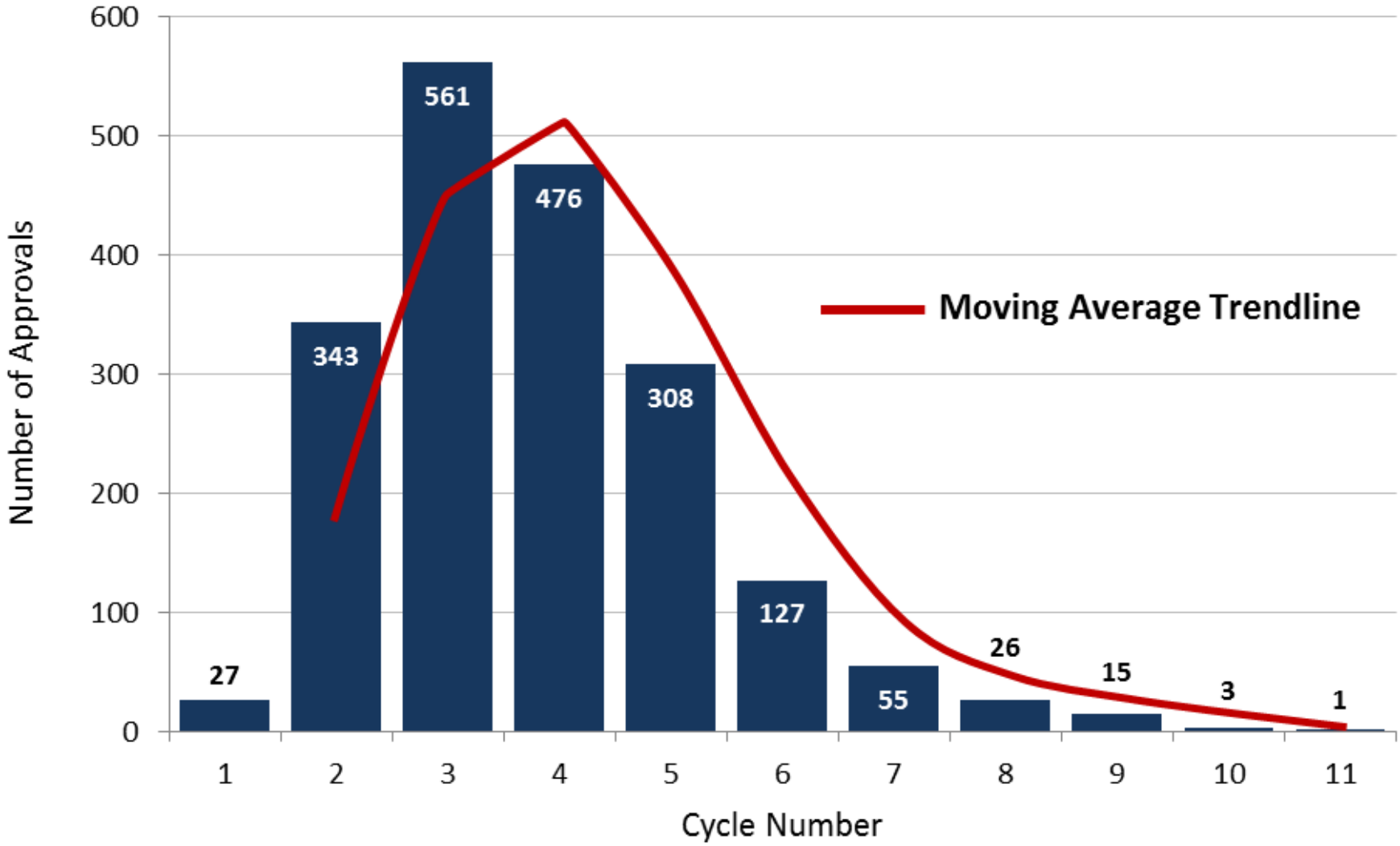
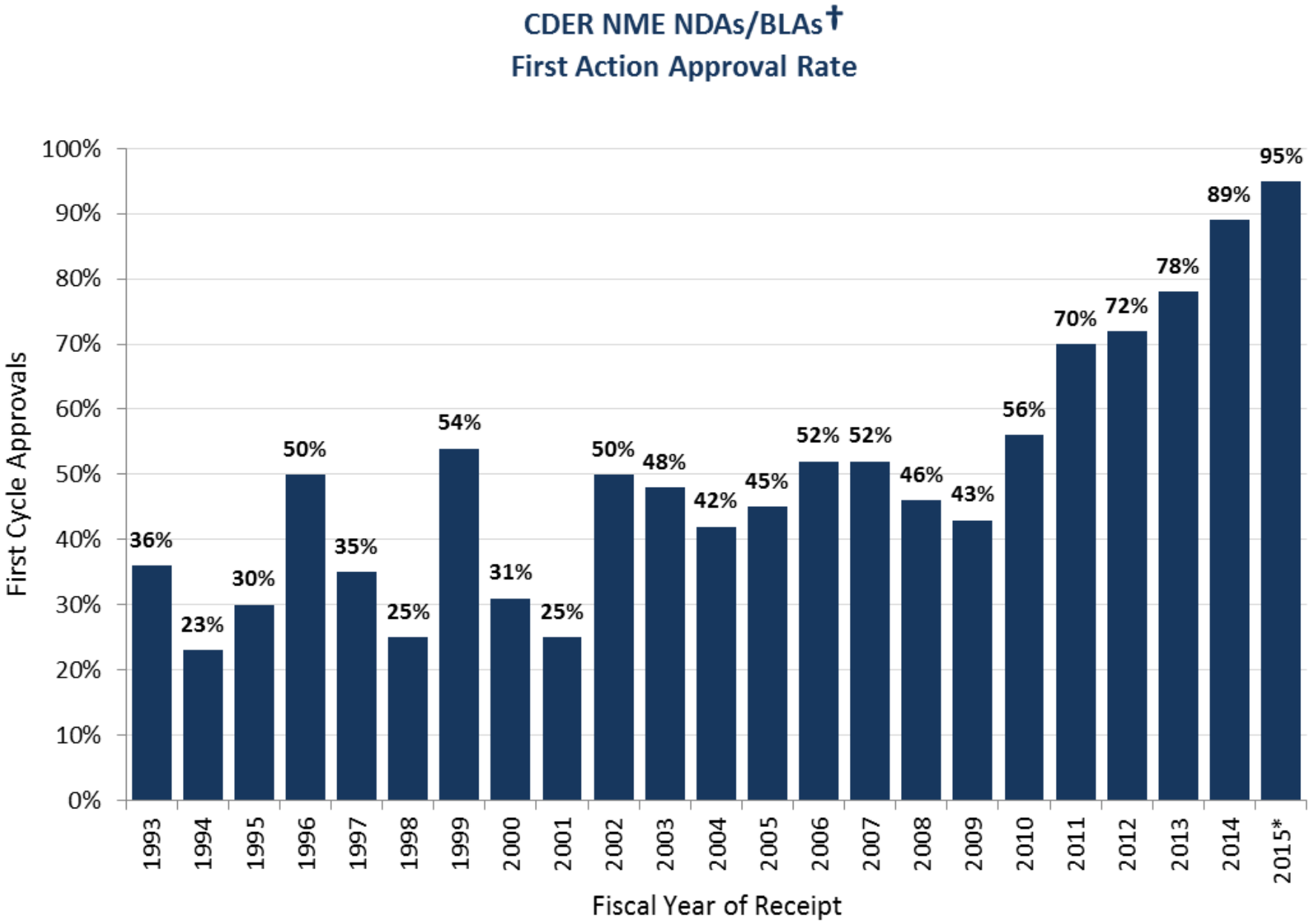
CMC Review Cycles for ANDAs to Approval

2009 through July 2014



First Cycle Approval Rate Under PDUFA



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4. **Update on Pre-Year 3 cohort**

COMMUNICATIONS ENHANCEMENTS FOR PRE-YEAR 3 ANDAs

(non-goal date applications)

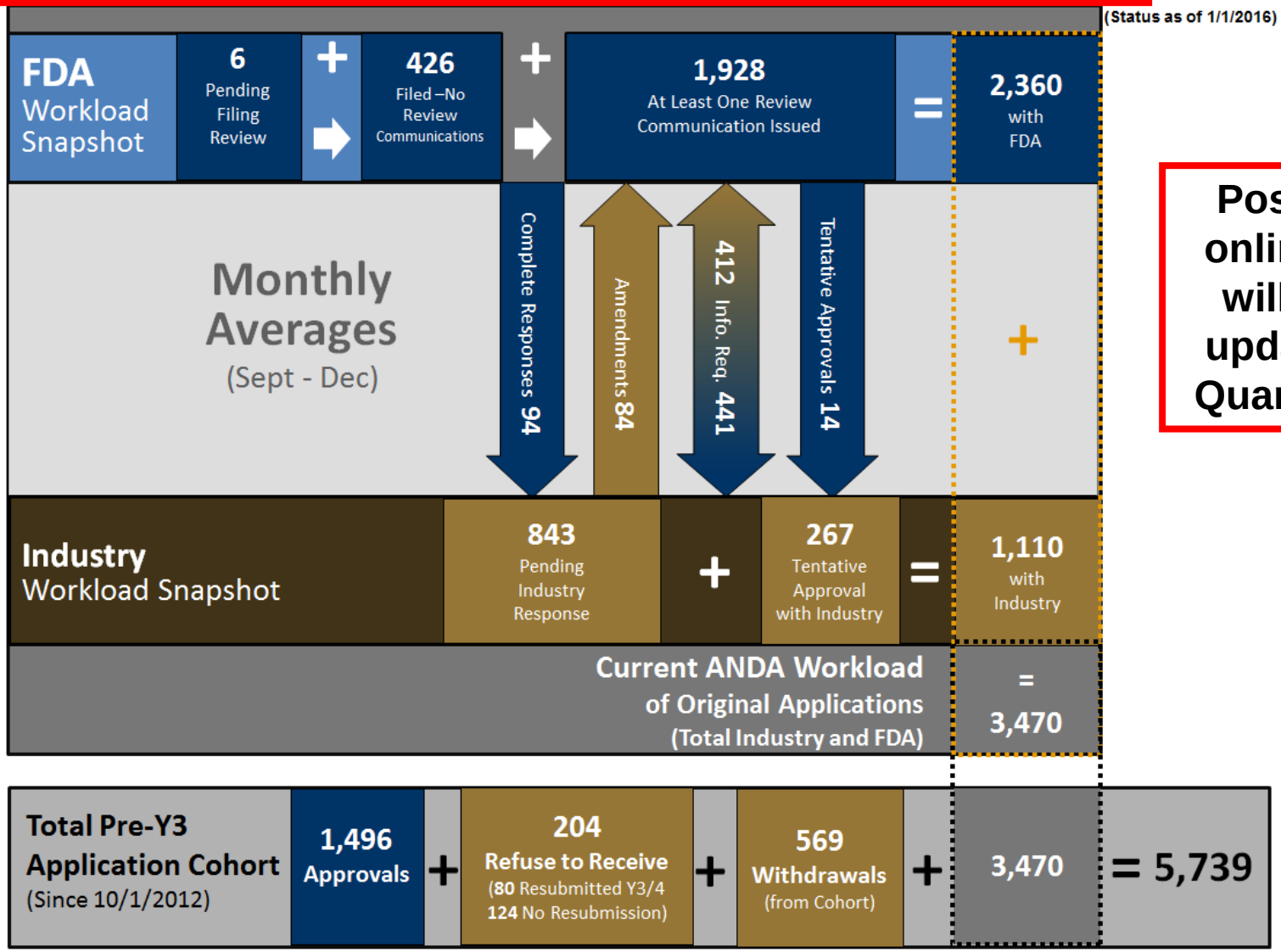
- Complete Responses pending inspections
- Information Requests (IRs), Easily Correctible Deficiencies (ECDs) and Real Time Communication
- Target Action Dates (TADs) assigned & communicated to industry
  - TLC for 1st generics to align with patent or exclusivity expiration
- Updated Communications with Industry MAPP to formalize and clarify these changes for pre-Year 3 applications
  - http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm369599.pdf

PREDICTABILITY for INDUSTRY

TADs for Additional Cycles (Pre-Year 3, non-goal date applications) similar to Goal date applications

Category	Pre-cohort Year 3 ANDAs	Pre-cohort Year 3 ANDAs (expedited status)
Major (CR)	10 months	7 months
Minor (CR)	5 months	3 months
ECD	3 months	
IR	3 months	

GENERIC DRUG REVIEW DASHBOARD
Pre-Year 3 ANDAs
(LAUNCHED 2/5/16)



Posted online & will be updated Quarterly

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm484609.htm

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CONCLUSIONS

YEAR 3 METRIC GOALS
How are we doing?

- GDUFA Backlog – FDA is way ahead of schedule – 86+% have received 1st action
- PASs – FDA is exceeding goals
- Controls – FDA is exceeding goals

YEAR 3 METRIC GOALS
How are we doing?

- ANDAs – too soon to tell; we are confident
- Amendments – too soon to tell; we are confident

- Application "Approvability" – too soon to tell

  (not a GDUFA metric)

WHAT IS NEXT?

Years 4 & 5:

- Review metrics tighten
- There will be up months and down months, but overall productivity on pre-Year 3 submissions will continue to increase

Strong focus on:

- TADs and related communications
- *First generics*: Avoid FTF PIV forfeitures, pursue timely first generic approvals

REAPING THE BENEFITS

- FDA is fulfilling its GDUFA commitments
- In many cases, we are going above and beyond our negotiated commitments
- We are building a robust, modern generic drug regulatory program
  - Sustainable and predictable
  - Clear and consistent communication
  - Fairness across applications and applicants

THANK YOU!