

CDER 2016 Actions and 2017 Priorities

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Disclosure

- My comments today are mine and do not necessarily represent the views of the US Food and Drug Administration



2016 ACCOMPLISHMENTS



CDER Operates Multiple Large Programs

- New drug regulatory program
- Generic drug regulatory program
- Biosimilar drug regulatory program
- Marketed drug safety surveillance
- Marketed drug quality oversight
- Compounded drug quality and safety
- Drug shortage program
- Drug supply chain oversight:
 - Track and trace
 - Imports (with ORA)
 - Unapproved drugs

CDER PDUFA Review Performance



Submission Type	FY 2015		FY 2016	
	Number Filed	Performance (Current)	Number Filed	Performance (Potential)**
Priority NME NDAs/original BLAs	24	92%	20	100%
Standard NME NDAs/original BLAs	22	100%	17	100%
Priority non-NME NDAs/BLAs*	9	100%	11	91%
Standard non-NME NDAs/BLAs*	84	95%	74	99%
Class 1 NDA/BLA Resubmissions	6	100%	5	100%
Class 2 NDA/BLA Resubmissions	35	97%	31	100%
Priority Efficacy Supplements	52	94%	45	100%
Standard Efficacy Supplements	123	94%	110	97%
Class 1 Efficacy Resubmissions	0	--	2	100%
Class 2 Efficacy Resubmissions	10	60%	10	90%
Prior Approval Mfg Supplements	544	91%	560	96%
CBE Mfg Supplements	1237	95%	1109	99%

Data as of 9/30/2016

*Beginning in FY 2013, the new tracked metrics are non-NME Priority and non-NME Standard NDAs.

† Includes submissions pending filing.

**Potential Performance refers to the level of performance that could potentially be achieved if all the actions currently pending are reviewed within their required goal date. Submissions with unknown review schedules are excluded.

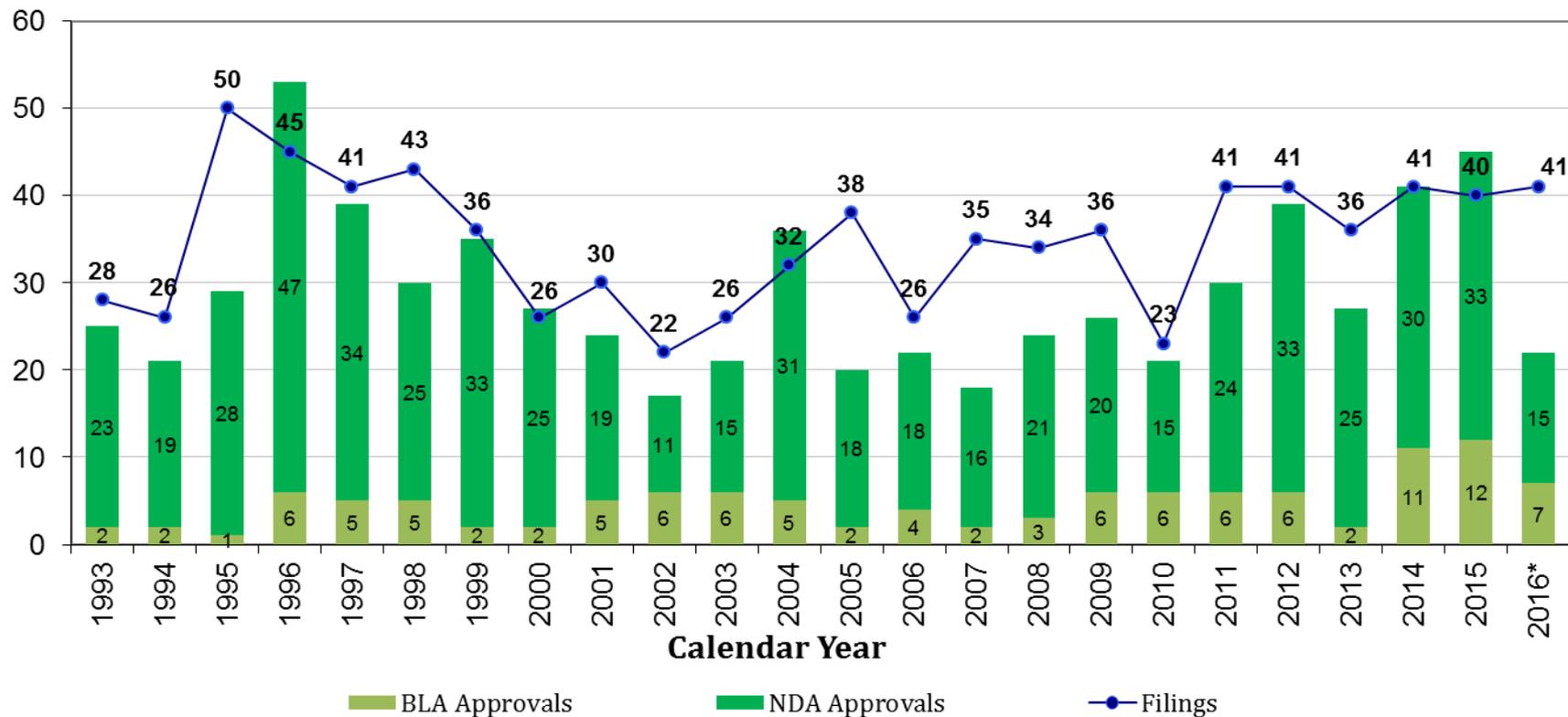
What About Novel New Drug Approvals?

- For CY16, through **December 31st, 2016**, CDER has:
 - Received **41** NME applications; average NME filings for past decade is 35
 - Approved **22** NMEs*, including **9** Orphan Drugs
- Reasons for fewer NMEs compared to CY15?
 - Approval of 5 NMEs in CY15 with CY16 due dates
 - Fewer NME actions in CY16
 - Increased number of CR letters in CY16

* This information is accurate as of December 31st, 2016. In rare instances, it may be necessary for FDA to change a drug's new molecular entity (NME) designation or the status of its application as a novel new biologics license application (BLA). For instance, new information may become available which could lead to a reconsideration of the original designation or status. If changes must be made to a drug's designation or the status of an application as a novel BLA, the Agency intends to communicate the nature of, and the reason for, any revisions as appropriate. This note applies to all references to NME/Original BLAs in this presentation.

CDER NME NDAs/BLAs[†]

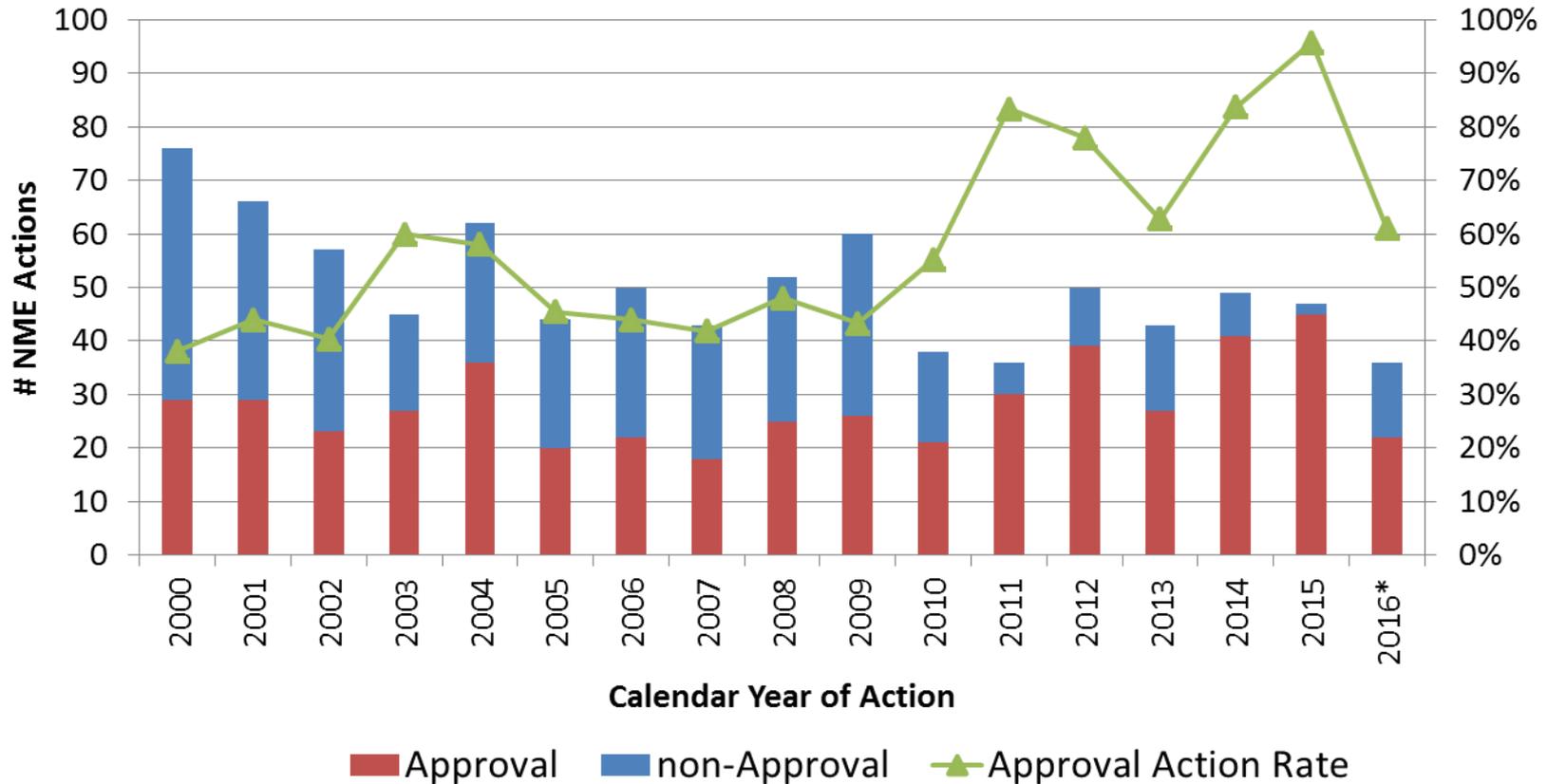
Filings and Approvals as of 12/31/16



[†] Multiple applications pertaining to a single new molecular/biologic entity are only counted once. Original BLAs that do not contain a new active ingredient are excluded. This information is accurate as of December 31st, 2016. In rare instances, it may be necessary for FDA to change a drug's new molecular entity (NME) designation or the status of its application as a novel new biologics license application (BLA). For instance, new information may become available which could lead to a reconsideration of the original designation or status. If changes must be made to a drug's designation or the status of an application as a novel BLA, the Agency intends to communicate the nature of, and the reason for, any revisions as appropriate. This note applies to all references to NME/Original BLAs in this presentation.

*Since applications are received and filed throughout a calendar year, the filed applications in a given calendar year do not necessarily correspond to an approval in the same calendar year. Certain applications are within their 60-day filing review period and may not be filed upon completion of the review.

NME Actions and Approvals



*Data as of 12/31/2016

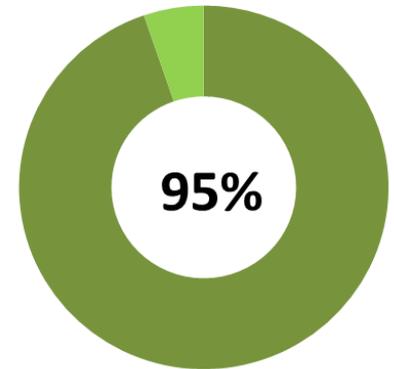
Includes discrete actions on a given date for an active ingredient which, if approved, would constitute a new molecular entity. Actions for original submissions and resubmissions as well as actions for new BLAs are included. Multiple actions which occur on the same date for multiple dosage forms or indications are counted as a single regulatory action.

In CY 2016, CDER Continued To Ensure The Efficiency Of First Cycle Review

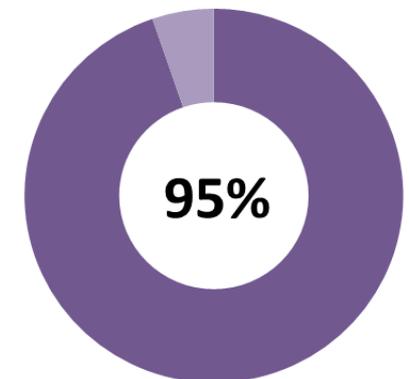


- All but one (95%) of the novel drugs approved to date in CY16 met their PDUFA goal dates for the approval review cycle
- Almost all (95%) of the novel drugs approved to date in CY16, were approved in the first review cycle

Met PDUFA Goal Date



Approved on First Cycle

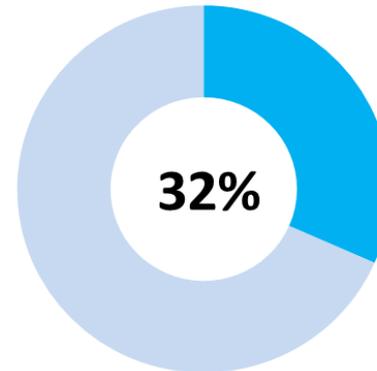




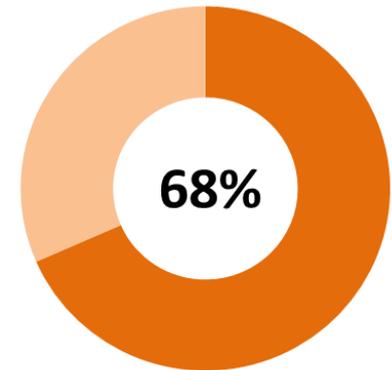
CDER Ensures That Novel Drugs Receive Expedited Review

- About Two – thirds (68%) of the novel drugs approved to date in CY16 were approved under Priority Review
- Almost a third (32%) of the novel drugs approved to date in CY16 received Breakthrough Therapy designation
- About four out of ten (36%) of the novel drugs approved to date in CY16 received Fast Track designation

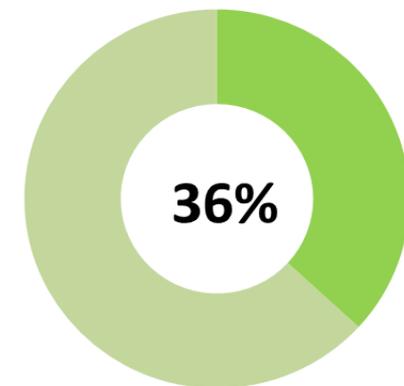
Breakthrough Therapy



Priority Approval



Fast Track



2016 Continues A Strong Track Record For Drug Innovation

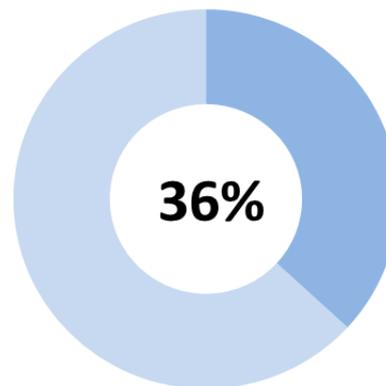


- Over a third (41%) of the novel drugs approved to date in CY16 are for rare diseases

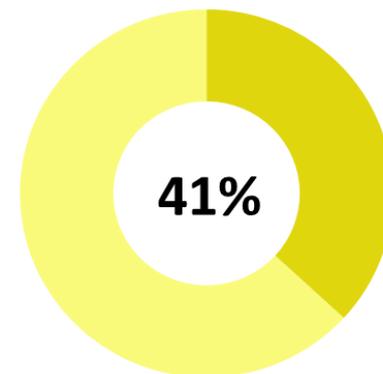
Almost four out of ten (36%) of the novel drugs approved to date in CY16 are the first in their class

About nine out of ten (86%) of the novel drugs approved to date in CY16 were first approved in the U.S.

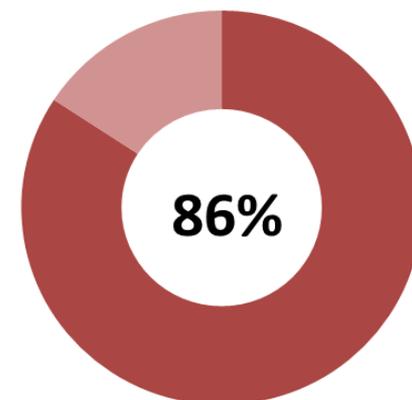
First in Class



Orphan Drugs



Approved First in the United States



Generic Drug Program

- FDA meeting or exceeding all GDUFA I goals
 - Current review goal - 10 months from the receipt of a new ANDA
 - GDUFA I commitment - take first action on 90% of ANDAs and PASs in “GDUFA backlog”
 - Surpassed this goal in 2016, more than one year ahead of schedule
- CY 2016 approvals
 - 813 approvals and tentative approvals – highest number on record
 - 630 approvals and 183 tentative approvals
 - 73 first generics
- CY 2017 approvals
 - 81 tentative and full approvals in March – 2nd highest month on record
 - 174 approvals (as of March 31, 2017)
 - Up from 154 in 2016 and 71 in 2015

Generic Drugs: Guidance

- Product-specific guidances (PSGs)
 - 158 new and 91 revised in CY 2016
 - Many involved complex dosage forms, such as inhaled powders, nasal sprays, topical products, and ophthalmics
 - More than 1,500 available, posted on [FDA's website](#)
- High rate of adequate bioequivalence reviews due to availability of PSGs
 - 70% of bioequivalence studies submitted* were found approvable by FDA on the first cycle

*data from Oct 2014 - Jan 2015

Generic Drugs: Advice

- 6,500+ controlled correspondences (“controls”) submitted since GDUFA began
 - Controls: communications from industry seeking written advice on an issue from the FDA
- Advice in controls improves application quality, hopefully decreases review cycles
- FDA has exceeded all GDFUA goals for controlled correspondences
 - Consistently responding to more than 90% of all controlled correspondences by the GDUFA goal date

Generic Drugs: Regulatory Science

- GDUFA funded research with significant impact on generics
 - Improve product development and understanding of bioequivalence for complex products
 - Testing innovative methodologies to determine bioequivalence for dosage forms that currently require clinical endpoint bioequivalence studies
 - Bioequivalence studies in patient groups (e.g., patients with epilepsy) where treating physicians had skepticism about use of generics
- FDA workshops and public meetings
 - Topics to include modeling and simulation, complex drug products, and topical products

Biosimilars Program



- Continue to approve biosimilar drugs: currently 5 approved
- Nine firms have publicly announced submission of a total of 14 351(k) applications
- “Biosimilars Development Program” contains 66 projects
- CDER has interacted with sponsors of biosimilars to 23 different reference products
- To implement the BPCI Act, FDA has finalized six guidances and issued four draft guidances.
- Still working on certain guidances

Drug Safety Operations

- Sentinel system has been integrated into routine postmarketing safety activities
- Modernized adverse event intake and triage operations to make them virtually paperless (involving more than 1.5 million reports)
- Consolidated human factors studies for drug-device combo products in OSE/CDER
- Working on “IMEDS” initiative: a Reagan-Udall Foundation portal for external use of Sentinel infrastructure



Drug Quality Program

- Have successfully developed a reliable inventory of world-wide facilities producing drugs for the US and have implemented risk-based inspection program
- Negotiating, with Global Operations Office, a Mutual Reliance Agreement with Europe on facility GMP inspections
- OPQ Office fully functional after massive reorganization
- Stimulating advanced manufacturing and emerging technologies (continuous manufacturing, 3D printing, etc)



Compounding Program

Since enactment of the DQSA on November 27, 2013, FDA has:

- Conducted approximately 425 *inspections* of compounders.
- Overseen over 90 *recall events* by compounders, and requested numerous compounders to cease operations
- Issued over 130 *warning letters*; one addressed violations identified at four facilities
- Issued over 30 *letters* referring findings from inspections of pharmacies that compounded their drugs in accordance with the conditions of section 503A to the states
- Obtained 4 *civil consent decrees* of permanent injunction
- Sought several criminal prosecutions



Other compounding actions

- Issued over 20 guidance documents
- Issued final rule and proposed rule describing additions and modifications to the Withdrawn or Removed List (503A and 503B)
- Solicited nominations for 503A and 503B bulks lists and for drugs that are difficult to compound under sections 503A and 503B
- Issued a proposed rule on the list of bulk drug substances that can be used to compound drug products
- Held 6 meetings of the Pharmacy Compounding Advisory Committee
- Held 4 sets of listening sessions with over 75 stakeholders
- Held 4 intergovernmental working meetings with the states

Inspection observations and serious adverse events



- Continue to identify insanitary conditions at many of the compounding facilities inspected
 - Dog beds and hairs in close proximity to sterile compounding room
 - Dead bugs in ceilings
 - Renovations being made without evidence of controls to prevent contamination
 - Compounding by personnel with exposed skin
- Continue to receive reports of serious adverse events and product quality defects, including contamination, related to sterile and non-sterile compounded drugs
 - Three infants administered superpotent (2460 %) compounded injectable morphine sulfate, which can cause respiratory depression, coma, and death
 - Fifteen patients developed bacterial bloodstream infections, and two patients died, from an infusion of contaminated calcium gluconate compounded in a facility where FDA observed insanitary conditions

Compounding Website and Progress Report



- For more information about FDA's compounding program, see
 - FDA's compounding website:
<https://www.fda.gov/drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/>
 - FDA's Human Drug Compounding Progress Report: Three Years After Enactment of the Drug Quality and Security Act (January 2017)



Progress on 2016 Priorities

- Have negotiated PDUFA, GDUFA, and BSUFA programs with industry and presented to Congress within required timeframes
- Have also made significant progress on OTC monograph reform and accompanying use fee program
- Implemented Opioid Action Plan activities
- Have met all goals of Sunscreen Innovation Act; have issued 4 final guidances and one final rule
- Patient-focused drug development: more than 20 total meetings; external groups also holding these

Progress on 2016 Goals

- Drug-resistant organisms:
 - Discussion of novel trial designs
 - Relevant provisions in “21st Century Cures”
- Combination product review: formation of Combination Product Council (Agency Level)
- ICH: Successful progress of re-engineered organization
- Biomarker qualification: progress with external stakeholders on evidentiary criteria

CDER 2017 Priorities

- Development and implementation of 5 year plan for process automation
 - Staged implementation of “Pharmaceutical Platform” now being used for generic drug review process
 - Formalization of IT governance
 - Formalization of data standards governance
- Successful re-authorization of 3 existing user fee programs
- Participate in process to evaluate modernization of OTC monograph process and potential user fee program support

CDER 2017 Priorities

- Continue to modernize facility assessment
 - Work with ORA on “PAG” agreements and their re-organization
 - Continue work on mutual reliance with EU
- Implement drug provisions of the 21st Century Cures Act
- Continue work on all fronts with respect to prescription opioid abuse

CDER 2017 Priorities

- Hiring: still many hundreds of positions below ceiling but making progress
- Continued implementation of recent statutes and user fee agreements
- Continued attention to designated “breakthrough therapies”
- Work with CBER and CDRH on implementation of “Oncology Center of Excellence”

CDER 2017 Priorities

- “Evidence Generation”
 - Recent article on “Real World Evidence” by FDA authors in NEJM offering a framework for thinking about regulatory use
 - Series of workshops with Duke Margolis Center for Health Policy on technical topics related to use of data collected in clinical practice to inform regulatory decisions
 - Multiple internal activities at FDA and with NIH intended to advance the field

Summary

- CDER made significant progress on its 2016 priorities
- 2017 will bring a new set of challenges
- Continued user fee (or other) support will be needed for program to meet its many obligations
- Planning to implement more automation and process re-engineering to improve efficiency