CDER 2016 Actions and 2017 Priorities

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2016 ACCOMPLISHMENTS

CDER Operates Multiple Large Programs

- New drug regulatory program (Dr. Jenkins)
- 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

2016 Generic Drug Program

- FDA meeting all GDUFA goals; current review goal 10 mths
- Successful implementation of “Panorama” for generic drug review program
- OGD has approved about 70 first-time generics, including drugs for many important indications, in the program
- Highest number of approvals and tentative approvals on record in 2016
  - 651 approved
  - 184 TA’d
- GDUFA commitment: take first action on 90% of ANDAs and PASs in “backlog”
  - Achieved this summer, more than one year ahead of schedule
  - Exceeded goal of 90%

Generic Drugs: Guidance

- In 2016, OGD issued 126 new and 73 revised product-specific recommendations (PSRs)
- Many involved complex dosage forms such as inhaled powders, nasal sprays, topical products and ophthalmics
- These PSRs are very helpful to industry: data from Oct 2014 thru Jan 2015 show that 70% of bioequivalence studies submitted were found approvable on the first cycle

Generic Drugs: Advice

- Since beginning GDUFA, industry has submitted over 5,400 “controlled correspondences”, by which they seek written advice on an issue from the FDA
- 2016 saw 1,883 of these
- FDA is meeting goals for responding
- This advice improves application quality and it is hoped will decrease cycles

Generic Drugs: Regulatory Science

- FDA funding research with significant impact on generics:
  - Testing mechanisms to determine bioequivalence for certain dosage forms that currently require clinical equivalence studies
  - Bioequivalence studies in patient groups (e.g., people with epilepsy) where treating physicians had skepticism about use of generics

Biosimilars Program

- Continue to approve biosimilar drugs: currently 4 approved
- Eight firms have publicly announced submission of a total of 12 351(k) applications
- “Biosimilars Development Program” contains 66 projects
- CDER has interacted with sponsors of biosimilars to 21 different reference products
- 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 that 1.5 million reports)
- Consolidated human factors studies for drug-device combo products in OSE/CDER
- Established a lead for opioid safety in OSE
- 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
- 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

- 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

Progress on 2016 Priorities

- Have negotiated PDUFA, GDUFA, and BSUFA programs with industry and expecting them to be 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) and significant policy progress
- 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