

CDER Update

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2017: Busy Year

- High levels of applications and approvals in many premarket programs
- Implementation of cures and reauthorized UFs
- Ongoing opioid crisis
- Increased emphasis on competition
- Drug shortage exacerbation by hurricane activity
- Continuing implementation of DQSA

2018 CDER Priorities (Preliminary)

- Center-wide informatics implementation
- Implement CURES legislation
- Carry out reauthorized BSUFA, GDUFA, PDUFA and meet goals
- Improve hiring process (with OC)
- Take multiple actions regarding opioid crisis
- Further progress in regulating compounding
- New drug regulatory program modernization
- OTC monograph reform

Center-wide Informatics

- Review platform fully operational in generics program
- Working to implement for new drug review program this year
- Have put in place formal Center governance of informatics activities
- Challenging area: hope for improvements in work management, understanding capacity, knowledge management, data standardization
- Multi-year project, \$\$\$

21st Century Cures Implementation

- Real world evidence policy development
- Patient-focused drug development
- Drug development tools program
- New hiring authorities
- Antimicrobial drugs breakpoint information
- Novel trial designs
- Model-based drug development

Real World Evidence

- Intend to publish Real-World Evidence framework as stipulated in legislation. Framework will describe the steps towards common understanding/utilization of such data
- Working on harmonization of common data models and open standards for evidence development (with NIH and HHS/ONC); also collaboration with UCSF of source data capture from EHRs using standardized clinical research data
- Ongoing demonstration projects
 - IMPACT Afib
 - Study comparing outcomes of randomized clinical trials to RWE collected from claims databases

Patient-focused Drug Development

- Section 3001, Patient Experience Data
 - Clinical reviewers will be filling out a new section in the benefit/risk section to include a statement on any patient experience data submitted or utilized during a review
- Section 3002
 - Public workshop on Dec 18 for feedback on
 - Standardized nomenclature and terminologies for PFDD
 - Methods to collect meaningful patient input throughout the drug development process
 - Methodologic considerations for data collection, reporting, management and analysis of patient input
 - FDA will publish a discussion document prior to the workshop

Patient-focused Drug Development

- Will put up a web site to pull together various patient-related activities
- Will start a centralized process for non-application-related meeting requests
- PRO qualification process has been converted to CURES-mandated DD tools procedures
- Will have standardized processes to receive and respond to externally-developed “Voice of the Patient” reports and draft guidances
- Working with CTTI on patient engagement projects

Drug Development Tools

- Have adopted Cures-stipulated process for qualification of DDTs including PROs, biomarkers and clinical outcome assessments
- Responsibility placed in OND
- Set up senior management committee to oversee precedential decision-making processes (similar to breakthrough designation)
- C-Path Institute to be an independent body to provide advice and consultation to tool developers
- Workshop on evidence generation for qualification will be held; CDER working with FNIH on describing evidentiary criteria for surrogate endpoints
- CPIMs (Critical Path Innovation Meetings) continue to be a great vehicle for non-regulatory brainstorming on innovative ideas, including tools, trial design, and novel development programs

Hiring and Retention

- New hiring authorities in CURES currently being explored; expect implementation in 2018; Melanie Keller, CDER's exec officer, currently on detail to OC to work on this
- New process and authorities should bring some relief and improved hiring and retention to medical product Centers
- Recent independent evaluation and public meeting on FDA HR process (stipulated in PDUFA) revealed many of the ongoing problems FDA is facing

Implement Re-Authorized PDUFA, GDUFA and BsUFA Programs

- PDUFA and BsUFA goals don't have major alterations from prior program
- FDA has initiated various projects laid out in the goals letters for these projects
- GDUFA goals are challenging AND application rate continuously increasing
- FDA's Drug Competition Action Plan adds a number of projects to the OGD portfolio
- CDER expects to meet or exceed GDUFA goals

Facility Assessment

- Facility problems continue to plague GDUFA, PDUFA and BsUFA programs—a major reason for more application cycling
- CDER's OPQ/OC is currently implementing with ORA the new “concept of operations” for facility assessment based on the ORA reorganization.
- This comes with clear roles and responsibilities and timelines for completing actions after facility inspections and notifying firms of final classification of facility status.
- Still need better clarity about cGMP standards and expectations. NIPP project (new inspection protocol) has been slow due to multiple other obligations of staff.

Opioid Crisis

- Treating opioid use disorder: CDER just approved a once monthly depot form of buprenorphine
- Preventing new OUD: ongoing expansion of opioid REMS; education about appropriate pain management
- Ongoing evaluation of B/R of currently approved opioids
- Evaluation of additional methods to improve prescribing practices
- Naloxone: developing information needed for OTC use

Regulation of Pharmacy Compounding

- Continue to build framework to implement statute:
 - Pharmacy Compounding Advisory Committee
 - Multiple guidances to be issued
 - Rulemaking to follow
- Follow-up on outbreaks, reports of patient harm; issuing compounding risk alerts
- Working extensively with states and state Boards of Pharmacy

New Drug Regulatory Program Modernization

- FDA's new drug program a global leader: some say "the gold standard"
- Known both for rigor of assessment and timeliness
- Comprised of both pre-market review (IND and market application) and post-market regulatory oversight
- Just achieved successful re-authorization of PDUFA

New Drug Regulatory Program Modernization

- Multiple factors drive the need for change:
 - New, rapidly-evolving science
 - Targeted therapies and precision medicine raise new challenges
 - Changing societal expectations
 - Patient involvement in drug development
 - Expectation of transparency
 - Digital revolution and rise of RWE
 - Globalization of drug development and maturation of multiple drug regulatory authorities around the world
 - Pressures on society from rising drug spend and consequent new scrutiny of regulatory authorities' standards
 - Call for new structures at FDA, e.g. OCE
 - Multiple unfunded or partially-funded Congressional mandates

New Drug Program Modernization

- Changes not about speed of review (“faster” or “slower”) or about approval standards (“higher” or “lower”)
- Will work out more efficient and effective ways to accomplish the review work in order to:
 - Collaborate with the community to address unmet medical needs
 - Oversee the approved armamentarium—both for safety and for appropriateness
 - Ensure policy consistency in regulatory decisions across units
 - Work with international regulatory community on harmonizing standards
 - Keep up with the fast moving science
 - Improve the transparency of our work
 - Increase currency and number of disease-specific drug development guidances

OTC Monograph Reform

- Current OTC monograph system is outdated and almost unworkable
- FDA has little ability to respond to safety issues arising with monographed products
- No possibility of innovation—stopped at 1972
- Staffing (approx 18 FTE in division) not adequate for the many tens of thousands of products on the market
- FDA has been working with other stakeholders on a reform proposal

Additional Activities

- Regulation reform: ORP working on evaluating existing regulations for currency
- Continuing to implement provisions of Supply Chain Security Act
- Intend to issue further guidance on sponsor communications with payers, and on communications consistent with FDA-approved labelling
- Issue guidance on identifying subpopulations for targeted therapies
- Keep ahead of emerging drug shortages as possible
- And many more

Conclusions

- CDER continues to have a robust number of ongoing initiatives to complete in addition to our regulatory workload
- Recent focus has been on generic drug and drug quality programs
- Now most urgent focus is IT governance and new drug regulatory program
- Likely other crises will happen over FY 18
- Program must rise to the various challenges and continue to serve the public in multiple ways