CDER Priorities

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CDER has Multiple Important Priorities

- Diverse stakeholders: all have expectations that their priorities will be addressed (promptly!)
- Congress has provided ongoing priorities in Statutory form: FDAAA, FDASIA, DQSA, Sunscreen Innovation Act, appropriations bill language
- Operation of four user fee programs with multiple ongoing goal commitments
- All relate to underlying mission of ensuring an accessible supply of safe and effective drugs, and preventing introduction of unsafe, ineffective or counterfeit drugs

Front Burner Priorities

- Implement new (and clarified) statutory provisions on drug compounding (Jane Axelrad, lead)
- Meet GDUFA review goals that went into effect 10/1/14 and continue to reduce pending applications (≈ 3000 applications) (OGD lead)
- Continue standup of Office of Generic Drugs "super office", (OGD lead)
- Stand up Office of Pharmaceutical Quality (Implementation team, lead)
- Implement and continue to develop PAG agreements with ORA (Andy Kish, CDER lead)
- Implement new process, data and document management IT system (OBI lead, this is a big deal!)

Front Burner Priorities

- Respond as needed and participate as requested in "21st Century Cures" legislative activities (Bob Guidos, lead)
- Rapidly re-evaluate our regulation of drug advertising and promotion in light of current jurisprudence around the 1st Amendment (CDER OMP, OCC, OC OP lead)
- Execute immediate actions required by Sunscreen Innovation Act; develop longer-term implementation plan (Theresa Michele, lead)
- Respond to Ebola outbreak (Ed Cox, lead)
- Issue final guidance(s) on abuse-deterrent opioid formulations (working group lead)
- Improve staffing:
  - More than 600 staff vacancies
  - Recruiting for multiple executive positions

Important Priorities (in no order)

- Develop new "Sentinel" network (OMP lead)
- Continue to refine drug safety program (from FDAAA, Terry Toigo, lead)
- Implement biosimilars program (Leah Chrystl, lead)
- Implement statutory provisions related to the drug supply chain and "track and trace" (Ilisa Bernstein, OC, lead)
- Stand up new Division in OTS (ShaAvhree Buckman-Garner, lead)
- Continue to work on Drug Label Improvement Initiative (OMP lead)
- Continue to work on new scenarios for Over-the-Counter drugs (OMP lead)

Important Priorities

- Post routine demographic information about development programs for newly approved drugs (John Whyte, lead)

- Develop a strategic plan for managing drug imports (TJ Chrystl, lead)

- Continue to refine policies around personalized medicine (OTS, OND leads)

- Continue to develop policy approach to development of antimicrobials for drug-resistant organisms (antimicrobial task force lead)

Important Priorities

- Evaluate the impact of "Breakthrough Therapy" designation program (Medical Policy Council lead with OSP)
- Additional programs agreed to under PDUFA V
- Continue work on streamlining clinical trials (OMP lead)
- Evaluate approaches for additional indications for targeted cancer therapies (Oncology Office lead)
- Evaluate the impact of requiring CV safety studies for certain chronic indications, e.g., diabetes and obesity (OND lead)

Important Priorities

- Make significant progress on FDA-EU mutual reliance initiative (with GO, Dara Corrigan, lead)
- Continue to push standards development and standarized electronic submissions (Mary Ann Slack, lead)
- Continue to conduct, and assess impact of, patient-focused drug development meetings (OSP lead)
- Continue pilot of semi-quantitative benefit-risk assessment template and evaluate it (Patrick Frey, OSP, lead)
- Refine approach to PRO development (beginning to implement refined approach to biomarker qualification process)
- Issue important drug development guidances (OND)
  - Draft on Duchenne Muscular Dystrophy
  - Final on approaches to pre-dementia Alzheimer's

Important Priorities

- Advance progress of the more than 20 consortia CDER is collaborating with (OTS lead)
- Develop new sustainable model for ICH (T Mullin, lead)
- Work on ways to get drugs not supported by PREA/BPCA studied in children (OTS and Lynn Yao, OND)
- Develop implementation plan and training for pregnancy/lactation label rule (Maternal health staff)
- Further develop use of Bayesian statistics, adaptive designs, modeling approaches, etc. for difficult drug evaluation issues (Lisa LaVange, lead)
- Ones I can't talk about (because they are pre-decisional, under review, etc.)

Continuing Priorities

- These have been previous high priorities and they are continuing to perform well:
  - PDUFA process: meeting the goals
  - FOI : Reducing the backlog in the face of a higher request rate
  - Advisors and Consultants: holding AC meetings
  - OSE operations: multiple safety functions
  - CDER research functions: well-organized, integrated with regulatory staff, and productive

Important Administrative/Managerial Priorities

- Re-evaluate CDER governance system (ongoing, Mary Beth Clarke, lead)
- Develop a more mature quality management system (JW lead)
- Refine time reporting system (OSP lead)
- Fully implement new training model (Kathy Hanson, DTD, lead)
- Build in-house OD capacity; continue OD efforts in new OGD and OPQ (Kathy Hanson)
- Continue to look at root causes for Employee Viewpoint Survey Results lowest scores (CDER generally gets excellent scores overall in this survey) (OEP, lead)

FURTHER INFORMATION ON SELECTED PRIORITIES

GDUFA Goals

- CDER has met GUDFA goals so far
- Action date goals went into effect 10/1/14 for newly filed applications
- These are being managed in new IT system and are all on track
- OPQ will perform "real time" interactions with generic drug sponsors to answer easily resolved questions in a timely manner; OGD goal is to minimize cycling
- Choke points in process identified and being dealt with
- Expect excellent performance around newly submitted application goals

GDUFA Goals

- Submissions pending prior to 10/1/14 must have first action prior to end of 5 year program
- Clearly, can't do all 3000+ original submissions at once or all at the end: must stagger. Have dealt with many thousands of pending supplements
- Prioritizing patent expiry, first generics, paragraph 4 etc. but also must migrate into IT "platform" and assure correct dates
- Sponsors should be hearing from FDA with questions on many of these applications over next year

Standup of OGD "Super-Office"

- Re-organization carefully planned to support critical functions of generic drug review
- Several key leadership positions filled
- Controlled correspondence and policy functions working well
- Working through administrative roadblocks to generic approval via "Drug Lifecycle Council"
- Several public meetings on research agenda

Standup of Office of Pharmaceutical Quality

- Slated for Jan 11, 2015
- Two years of planning structure and implementation
- Centralizes quality review for new and generic drugs
  - New and lifecycle drug product offices
  - Office of Process and Facilities with microbiology, process, and facility inspection divisions
  - Office of Surveillance for post-market inspections and surveillance in conjunction with ORA
  - Centralized project management—largest throughput office in Center
  - Policy and Research Offices

OPQ: New Surveillance Function

- Seeks to identify quality status of all facilities manufacturing drugs for US market
- "Pharmaceutical Platform" IT system will support: links ORA and CDER databases
- Integrate intelligence from many sources: applications, inspections, "quality metrics"
- New quantitative template for inspections being developed by ORA and CDER—scoring system to include "exceeding" minimal expectations as well as not meeting. Risk based.
- Surveillance Office will integrate all the info in a risk model to target inspections

New Surveillance Function: Quality Metrics

- Intend to collect well-understood metrics from facilities regarding state of quality

- Metrics widely used in quality management in most large-scale manufacturing sectors

- Often combined in ''dashboard'' to alert management to impending problems

- Takes time to understand metrics and make sure they represent the same measure across various groups; pilots ongoing

CDER-ORA PAG Agreement

- Integrate ORA facility pre-approval inspections into OPQ team review—one overall quality assessment. Pilots ongoing; new inspectional template under development
- Specialized pharmaceutical inspectional personnel in ORA will work closely w Center
- Share data from various systems seamlessly
- CDER hopes to provide tablets or other handhelds to streamline report generation

New IT System

- Workflow management, data and document management components
- Plan to implement in all Center processes over multi-year process
- Will replace DAARTS!!
- "Pharmaceutical Platform" will begin to instantiate wish list of quality reviewers. Has already replaced multiple non-connected databases
- Usual bumps encountered as we conduct major re-org, implement new review goals and stand up new IT system all at once. We will get through it.

Safety Functions

- New Sentinel Network
  - New contract completed for Sentinel Network (no longer "mini")
  - Currently contains data from 178 million lives
  - Need to institutionalize system as a standard tool in marketed drug safety evaluation
  - Methodologic research also being carried out by IMEDs (PP Partnership via Reagan-Udall Foundation)
- Refining approach to REMS, etc.
  - Policy work (Terry Toigo, lead)

"Drug Snapshots": Demographic Information on Development Programs

- Commitment in Action Plan from FDASIA 507
- Post info on participation in trials by sex, race, age and ethnicity
- Posted pilot group of certain NMEs from 2014; opened docket and seeking comments on presentation of data
- Not as easy as it looks!!
- Low representation of certain racial/ethic groups in trials: multiple factors contribute
- How much is enough??

"Personalized Medicine" Policies

- CDER is approving significant number of "targeted therapies"
- These drugs target pathways or specific genetic mutations and thus are less disease-specific
- Target populations tend to be narrow sub-populations of specific diseases; and developers then seek to get additional indications
- Efficacy requirements for these additional "small slices" are under consideration. Have used case-by case evaluation up to now, but broader policy development is needed
- Workshop 12/12/14 at White Oak on this topic

Streamlining Clinical Trials: Multiple Projects Ongoing

- Collaboration with CTTI on trial innovation
- Use of new IT
  - Use of personal devices for patient input
  - Use of telemedicine in clinical trials
- "Monitoring and Data Cleaning Practices":
  - Traditional monitoring may not be most effective way of ensuring data quality: building quality in; developing risk-based approaches, and focusing on the most important data points may provide better quality

Evaluation of Breakthrough Therapy Designation Program

- Pace of submissions and designations continue
- Initial evaluation of 1st two years conducted by OSP
- Surveyed medical staff; did not survey industry
- We seek both process and content improvements
- Industry input will be helpful in determining the value of the program: did it help and, if so, how was the designation helpful? Evaluation will be done under contract.

Evaluation of Breakthrough Drug Program

- Clearly, for some new drugs, designation accelerated availability to patients
- Lack of clarity for industry leads to many requests that are not on the mark
- Large volume of turndowns increases workload for medical review staff, without any payoff
- We are working to streamline process for requests that clearly don't qualify

"Patient-focused" Drug Development

- Series of 20 patient-focused meetings agreed to under PDUFA V

- FDA continuing to develop B/R assessment framework that incorporates burden of disease (hopefully with patient input)

- These are going well, but it is clear that these initiatives reflect a broader trend that is gaining traction

- Question arises over next steps

"Patient-focused" Drug Development

- We understand that people with chronic diseases are "experts" in that disease, as far as the symptoms and the impact on QOL, and what might be acceptable tradeoffs
  - On risk
  - On uncertainty
- How to meaningfully collect that knowledge, in rigorous manner, given that there is a spectrum of opinions and and a spectrum of disease burden in any given disease?
- How to do this for the many thousands of diseases?

"Patient-focused" Drug Development

- Many patient groups and non-profits getting involved in evaluating these issues

- For FDA/CDER, we must assess how such input can be translated into acceptable endpoints and drug development guidance

- Piloting, e.g., with PRO qualification process and with submission of draft guidances by patient/professional groups

Importance of Good Management

- In addition to these priority initiatives and other initiatives, CDER has a large volume of work that must be accomplished every day: we are a production shop
- Tens of thousands of decisions made yearly on INDs, applications and supplements; thousands of meetings with industry; more than 50 guidances and multiple regulations published; FOI work; AC's; import decisions; drug safety communications; underlying drug safety evaluation activities; evaluation of inspection results; compliance and enforcement actions; and scientific activities, to name just a few.
- Ensuring that all this gets done, well and efficiently, requires engaged staff members who feel supported and listened to by leadership, careful process and quality management, and high-quality IT support

Importance of Good Management

- Many of our stakeholders have policy priorities and do not understand how critical good management is to making things happen; seems to be a general problem in government
- It is feasible to handle a handful of initiatives through an informal process, but not hundreds, while at the same time managing the ongoing workload
- CDER's "lean team" assists with process improvement throughout the Center
- We have a plan for implementing modern IT process and data support: accomplishing these longer-term goals will be key to sustaining our success

Summary

- CDER has numerous priority initiatives for 2015 along with ongoing workload

- Outstanding progress has been made in many areas, but we are all quite pressed

- Large number of staff vacancies also require VERY significant amount of work to fill

- Attention to continuous improvement in management and IT support will enable accomplishment of a broad agenda