CDER Keynote Address

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Outline

- CDER's modernization roadmap
- Initiatives to facilitate access to generics and biosimilars
- Path to harmonization for generic drugs
- The importance of pharmaceutical quality
- Closing comments

CDER’s Modernization Roadmap

CDER's Modernization Roadmap

- Modernization of the new drugs regulatory program
  - Therapeutically focused divisions
  - Scientific expertise and leadership
  - Integrated and cross-disciplinary reviews and assessments
- Integrated operations
  - Financial management
  - Time reporting and capacity planning
  - Portfolio management
- Deployment of technology solutions
  - Application review workflow
  - Knowledge management
  - Knowledge-aided Assessment and Structured Application (KASA)

Deployment of Technology Solutions

Knowledge-aided Assessment and Structured Application (KASA) System

- Capture and manage knowledge - such as established conditions - during the lifecycle of a drug product
- Establish algorithms for risk identification, mitigation, and communication
- Perform computer-aided analyses of applications to compare regulatory standards and quality risks across approved applications and facilities
- Develop a structured format for the pharmaceutical quality/Chemistry, manufacturing, and control (PQ/CMC) information submitted in the generic drug product applications
- Enable consistency in the content of PQ/CMC data, and contribute to a more efficient and effective regulatory decision-making process

Initiatives to Facilitate Access to Generics and Biosimilars

Reducing the Hurdles for Generic and Biosimilar Access

- Drug shortages task force
  - Holistic solutions to address underlying causes
- Drug competition action plan
  - Increase competition in the market for prescription drugs and facilitate entry of lower-cost alternatives.
- Biosimilar action plan
  - Create a more competitive biosimilar market while creating greater incentives for sponsors

Drug Competition Action Plan (DCAP)

- Three prongs
  - Streamline ANDA review process to increase efficiency, effectiveness, and output of approvals
  - Enhance development and review of complex product ANDAs
  - Reduce “gaming” that delays generic approval and extends monopoly beyond what Congress intended
- DCAP aligns with GDUFA II main objectives
  - Reduce the number of review cycles to approval
  - Increase first-cycle approvals of safe, high-quality, and lower-cost generic drugs

Biosimilar Action Plan
Four Key Strategies

- Improve the efficiency of the biosimilar and interchangeable product development and approval process
- Maximize scientific and regulatory clarity for the biosimilar product development community
- Develop effective communications to improve understanding of biosimilars among patients, clinicians and payors
- Support market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition

Path to Harmonization for Generic Drugs

Why Harmonize in Generic Context?

- Absence of harmonized standards risks impeding generic drug global availability

- Potential benefits of future harmonization
  - Reduce the impact of different regulatory standard in different regions unique to generics
  - Reduce manufacturers' costs associated with meeting potentially duplicative regulatory requirements in different regions
  - Reduce the cost of regulatory oversight by providing regulators more opportunities for information sharing with their regulatory counterparts

Drug Harmonization Activities

- International Council on Harmonisation (ICH)
  - Unique venue for regulatory-industry expert work to harmonize scientific and technical standards
  - Over 60 completed guidelines, many (including all **Q**uality guidelines) apply to generic drugs
  - International Generic and Biosimilar Medicines Association (IGBA) participates as ICH Member and Elected Management Committee member (as of June 2018)
- International Pharmaceutical Regulators Programme (IPRP)
  - Promotes information sharing, best practices, cooperation, and regulatory convergence
  - Reflects 2018 merger of International Pharmaceutical Regulators Forum (IPRP) and International Generic Drug Regulators Programme (IGDRP)
  - Standing work groups include: Quality for Generics, Bioequivalence for Generics, and Information Sharing for Generics
- Direct work with other regulatory bodies
  - EC/EMA Bilateral discussions in June helping identify potential regulatory harmonization opportunities;
  - EMA and FDA fellowship exchanges further advance mutual understanding supporting future harmonization

The Importance of Pharmaceutical Quality

Facility Assessment and Surveillance Process Improvement

- Integrated quality assessments
- Quality metrics
- Mutual recognition agreement
- New inspection protocol project
- Concept of Operations for Facility Evaluation and Inspection

Mutual Recognition Agreement

- U.S. and EU regulators will be able to utilize each other's good manufacturing practice inspections of human pharmaceutical manufacturing facilities
- Represents culmination of more than four years of FDA/EU cooperation as part of the Mutual Reliance Initiative.
- Allows FDA and EU to rely upon information from drug inspections conducted within the countries' respective borders
- Enables FDA and EU to avoid duplications, increase efficiencies, leverage mutual resources and expertise and devote more resources to other parts of the world where there may be greater risk

New Inspection Protocol Project

- FDA-driven internal analysis and modernization of inspection protocols
- Focus on pre-approval and surveillance inspections of drug and biological products
- More structured streamlined electronic capture and automated reporting of investigator fact collection
- Explicitly address manufacturing quality and have the inspection include analyzable observations that better enable assessment of facility's state of quality maturity
- Starting with sterile dosage form inspections, expanding to additional dosage forms and all types of products
- Anticipate enabling enhanced quality surveillance and inspection planning

Concept of Operations Model Highlights

- Strategic alignment across CDER and Office of Regulatory Affairs (ORA) functional units
- Improved timelines for regulatory actions and communication with stakeholders
- Parity between domestic and international functions
- Improved collaboration, communication, and information sharing
- Streamlined work flow and processes
- Clear roles and responsibilities
- Better use of quality knowledge to support facility evaluation and inspection

Improving Quality is the Key to Increasing First Cycle Approvals

FIRST CYCLE ANDA APPROVALS¥

Prior to GDUFA	< 1%
FY2015	11.6%
FY2016	14.7%
FY2017*	~10%
FY2018**	TBD

*** Updated 5/1/2018.** Numbers are based on preliminary data that will be reviewed and validated for official reporting purposes. Some FY2017 ANDAs are under review and within goal.

**FY2018 – ANDAs are under review and within goal; the majority of FY2018 ANDAs have not reached their GDUFA goal date.

¥ DEFINITION: The percentage of AP and TA original and original-response to RTR ANDAs that were received for extensive review AND were given a regulatory decision (excluding ANDAs under review).

Closing Comments

- Modernization and technology-aided innovation
- Promote the availability of better medicines
- Strengthen partnerships and engage stakeholders
- Harmonization efforts need engagement and resources from both regulators and industry
- Shared responsibility and commitment for the quality of medicines