CDER Keynote Address

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Outline

- Improving patient access to affordable medicines
  - Increasing the availability of generic drugs
  - Advancing the development of biosimilars
- Patients expect reliably safe and effective medicines
  - The impact of suboptimal pharmaceutical quality
  - Strengthening pharmaceutical quality management systems
- Promoting the availability of better medicines through innovation
  - Modernization of quality management through multiple programs (overview)
  - Major technology initiatives/KASA

Beyond the Generic Drug Approval Numbers: Patient Impact

CDER's generic drug program protects public health by:

Maintaining a thriving generic drug assessment program	Approving and regulating safe, effective, high quality generic drugs	Monitoring generic drugs on the market to ensure safe, effective, high-quality medicines remain available to the public

Increasing the Availability of Generic Drugs

Advancing the Drug Competition Action Plan (DCAP)

- **Encourage robust and timely market competition** for generic drugs and
- **Help bring greater efficiency and transparency** to the review process:
  - Launched website – *Upcoming Product-Specific Guidances (PSGs) for Complex Drug Product Development*
  - Updated
    - *List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic*
    - *Reference Listed Drug (RLD) Access Inquiries* and
    - *Patent IV Patent Certifications List*
  - Issued 8 draft guidances, 1 final guidance, and hundreds of PSGs for industry
  - Held regulatory science workshops to support complex generic drug development

DCAP – Looking Ahead

- **Continue to provide applicants with greater clarity and transparency:**
  - Revised Q&A Guidance on 180-Day Exclusivity
  - Guidance on Active Ingredient Sameness Evaluations in ANDAs
  - Series of Companion Guidances on Characterization of Topical Dermatological ANDA Products
  - Revised Guidance on Bioequivalence Studies with Pharmacokinetic Endpoints for Drug Products Submitted in ANDAs
- **Work to ensure timely availability of therapeutically equivalent products:**
  - Q&A Guidance on the Orange Book
  - Foundational Guidance on Therapeutic Equivalence

Progress in Advancing the Development of Biosimilars

- Established the Office of Therapeutic Biologics and Biosimilars (OTBB) to further improve coordination and support of all activities related to biosimilar and interchangeable product development and approval
- Released several draft and final guidances to support the efficiency, quality, and predictability of biosimilar product review and development
- Held two public meetings to hear from stakeholders about biosimilar and interchangeable products, including one on developing biosimilar and interchangeable insulins
- Released educational materials for health care providers and patients

Biosimilars Action Plan (BAP): Looking Ahead

- An enhanced Purple Book is in development:
  - Improved interface to provide user-friendly information to the public about approved biologics
  - Enhanced information for patients, prescribers, pharmacists, and other stakeholders
- Develop new review template
  - Standardized review templates tailored for biosimilar and interchangeable products
- Update and modernize biological product regulations
  - Enhanced clarity and regulatory certainty
  - Help prevent “gaming” that could prevent or delay competition
- Additional guidance and educational materials will be developed

The Importance of Pharmaceutical Quality

- Pharmaceutical quality is what assures drugs *on the market* are safe and effective
- As we improve patient access to medicine, we cannot sacrifice quality
- When quality goes wrong, everything can go wrong

Inter-agency Drug Shortage Task Force
Drug shortages: root causes and potential solutions

Root causes

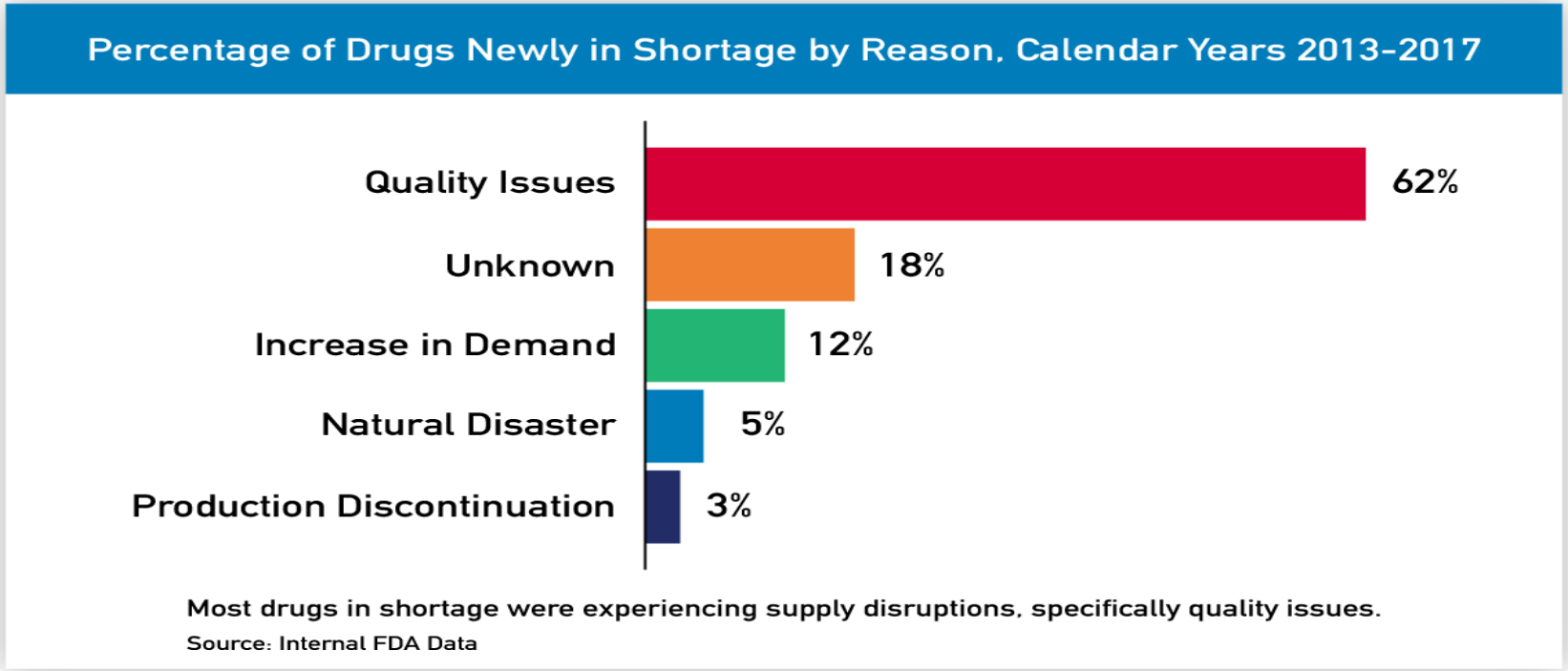
- Lack of incentives to produce less profitable drugs
- Market does not recognize and reward manufacturers for mature quality management systems
- Logistical and regulatory challenges make it difficult for the market to recover after disruption

Recommendations

- Create a shared understanding of the impact of drug shortages and the contracting practices that may contribute to them
- Create a rating system to incentivize drug manufacturers to invest in achieving quality management system maturity
- Promote sustainable private sector contracts

Report / Drug Shortages: Root Causes and Potential Solutions
https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

Quality issues: leading cause of drug shortages



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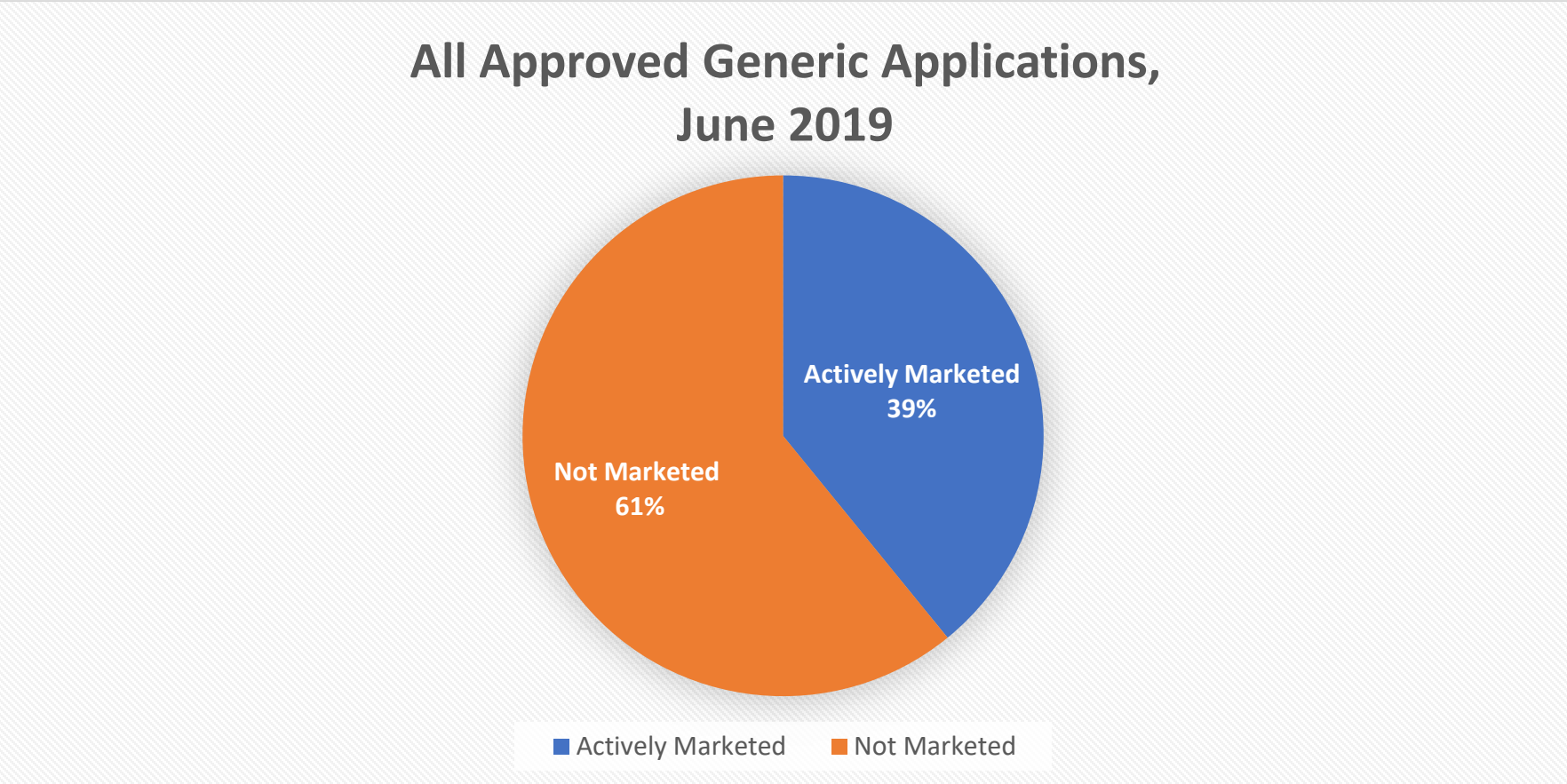
Not all approved ANDAs are marketed



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Manufacturers and those with oversight and controls over manufacturing must take ownership for quality

- Management sets the tone
- Invest in people
- Organizational objectives drive quality
- Quality systems shape culture
- Focus on innovation and continual improvement
- Move to performance-based quality management

Achieving quality management maturity

- A quality management system is a collection of business processes needed to consistently implement and maintain quality of product in the marketplace
- Basic quality management systems are generally more reactive and focused on-Current Good Manufacturing Practice (CGMP) compliance
- Stronger, more mature quality management systems are ones that proactively focus on performance, especially outcomes that affect the patient, including reducing quality issues that lead to complaints, shortages, and quality-related adverse events

FDA's Quality Metrics Program is intended to provide additional insight into products and facilities

Quality Metrics programs are part of a mature quality management system

FDA's Quality Metrics Feedback Program is open

- Solicits information from drug manufacturers that have implemented and are currently using quality metrics programs
- Any data shared is for demonstration/informational purposes only
- The program is open for meeting requests until Dec 30, 2019

Modernizing the FDA

Modernizing Programs

Investing in IT Solutions and Tools

Improving Inspections

CDER's Major Technology Initiatives

New Drug Review Modernization

- Effort to evaluate and transform new drug review processes
- Implementation of digital process automation tools to support IND and NDA/BLA review

Knowledge-Aided Assessment and Structured Application (KASA)

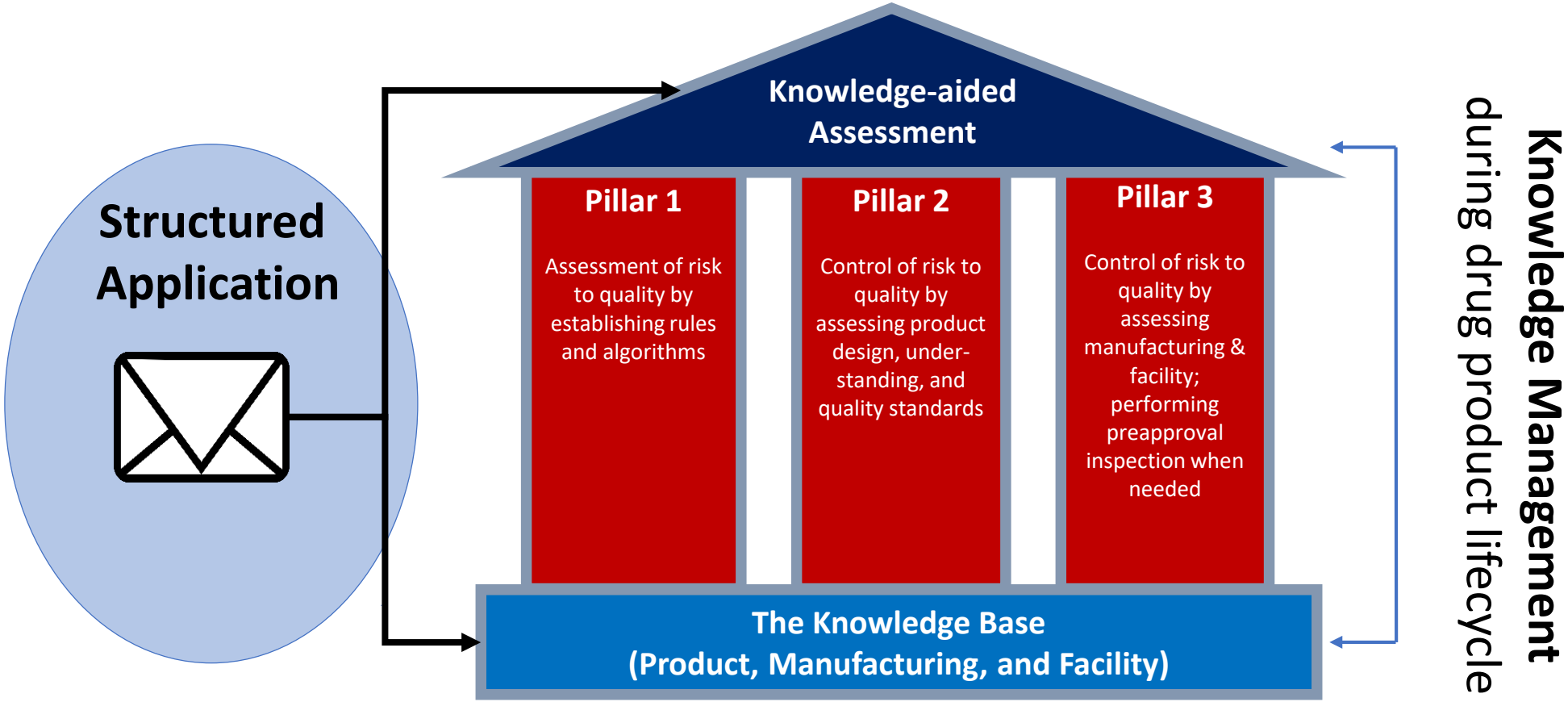
- Focus on content of regulatory quality assessment
- Inform regulatory decision making
- Capture and manage knowledge across products and facilities

Safety Lifecyle Signal Tracking

- Implementation of workflow automation tools to capture, track and adjudicate safety signals pre and post market.

The KASA System

KASA – Knowledge-aided Assessment and Structured Application



New Inspection Protocol Project (NIPP): The inspection paradigm also needs to evolve

- Inspections should gather analyzable data where possible – to inform on-going assessment of facility state of quality (effectiveness of quality management).
- Develop standards to more consistently gauge state of quality management maturity observed during inspection
- Develop a data-rich abbreviated inspection format and more structured, standardized inspection report.
- More readily accessible interpretable, and analyzable post-inspection, to better inform regulatory decisions

In conclusion:

- The value of the generic and biosimilar programs resides in their impact on reliable access to affordable, high-quality medicines that make a difference for patients

- Manufacturers' quality management systems need to mature, and the regulatory framework needs to adapt to facilitate this evolution

- We need to continue to invest in process modernization and technology that will make the submission and assessment of applications more consistent and efficient