U.S. FOOD & DRUG ADMINISTRATION

Advancing Drug Product Quality

Patrizia Cavazzoni, M.D.
Deputy Director for Operations
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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CDER's Modernization Roadmap: Some Highlights

- Modernization of the new drugs regulatory program
- Technology solutions

CDER's Modernization of the New Drugs Regulatory Program

- Therapeutically focused divisions
- Centralized project management organization
- Multidisciplinary, issue-based process for review of BLA/NDA
- Standardized first-in-humans and efficacy trial protocol review process and template

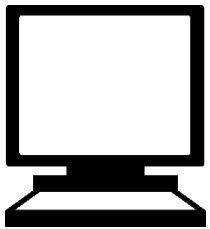
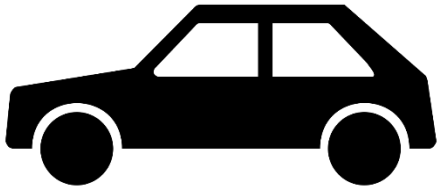
CDER's Technology Solutions

- IT portfolio organized around technology-enabled capabilities:
  - Application review
  - Knowledge management
  - Safety signal management
- Development of new IT platforms and applications

Pharmaceutical Quality

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.


Patients expect safe and effective
medicine with every dose they take.

Pharmaceutical quality is

manufacturing *every* dose to be safe and effective, free of contamination and defects.


It is what gives patients confidence
in their *next* dose of medicine.

Pharmaceutical Quality Oversight

new drugs

biologics

generics

compounded drugs

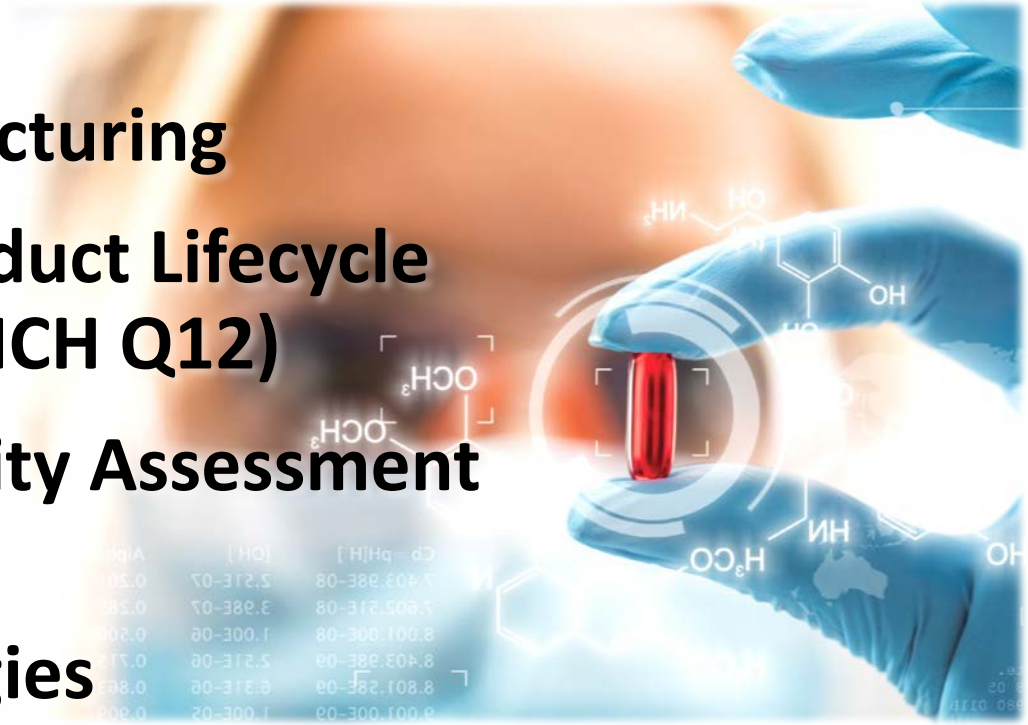
over-the-counter drugs

biosimilars

Development → Premarket → Postmarket

Major Quality Topics at this Conference

- Opioid Crisis
- Continuous Manufacturing
- Pharmaceutical Product Lifecycle Management (e.g., ICH Q12)
- Innovations in Quality Assessment (e.g., KASA)
- Emerging Technologies



Innovation:
Promoting Availability of Better Medicine


Innovation leads to better medicine.

We Want Innovation

Quality Metrics

- Quality Metrics Feedback and Site Visit Programs

Emerging approaches to pharmaceutical product design and manufacturing

- Emerging Technology Program

Complex generic products

- Pre-ANDA Program

Modernizing quality assessment with lifecycle knowledge management

- Knowledge-aided Assessment and Structured Application (KASA)

Modernizing quality assessment with standardized submission data

- Product Quality/Chemistry Manufacturing and Control (PQ/CMC)

Quality Metrics Programs

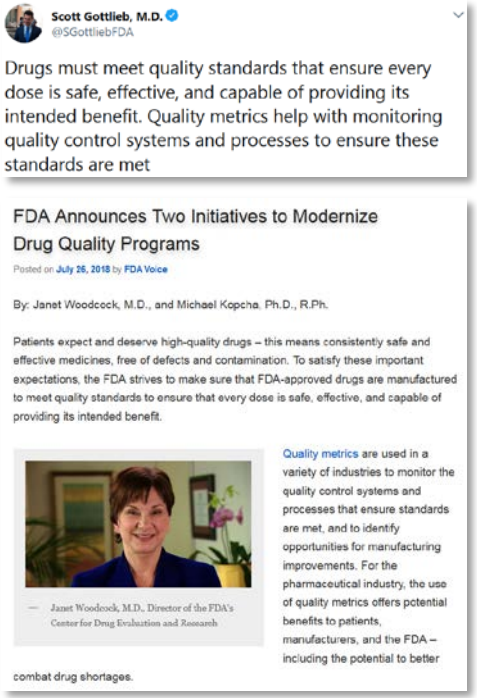
Quality Metrics

Many products are made using *Quality Metrics* to monitor quality control and continually improve quality.

Drugs *should be* no different.

FDA's Quality Metrics Programs

- **Feedback Program**
  - Solicits info from drug manufacturers using quality metrics programs for informational purposes only
- **Site Visit Program**
  - Provides on-site learning opportunities for FDA staff involved in the FDA Quality Metrics Program
- **"PhRMA also supports the current voluntary and pilot program approach to the Quality Metrics program."**
  - Public Comments on Docket No. FDA-2018-N-3272



Scott Gottlieb, M.D.
@SGottliebFDA

Drugs must meet quality standards that ensure every dose is safe, effective, and capable of providing its intended benefit. Quality metrics help with monitoring quality control systems and processes to ensure these standards are met

FDA Announces Two Initiatives to Modernize Drug Quality Programs

Posted on July 26, 2018 by FDA Voice

By: Janet Woodcock, M.D., and Michael Kopcha, Ph.D., R.Ph.

Patients expect and deserve high-quality drugs – this means consistently safe and effective medicines, free of defects and contamination. To satisfy these important expectations, the FDA strives to make sure that FDA-approved drugs are manufactured to meet quality standards to ensure that every dose is safe, effective, and capable of providing its intended benefit.

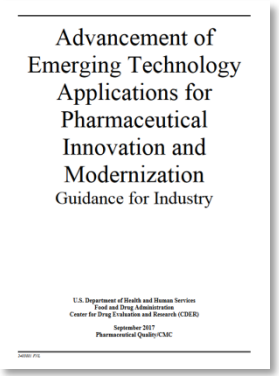
— Janet Woodcock, M.D., Director of the FDA's Center for Drug Evaluation and Research

Quality metrics are used in a variety of industries to monitor the quality control systems and processes that ensure standards are met, and to identify opportunities for manufacturing improvements. For the pharmaceutical industry, the use of quality metrics offers potential benefits to patients, manufacturers, and the FDA – including the potential to better combat drug shortages.

Emerging Technology Program

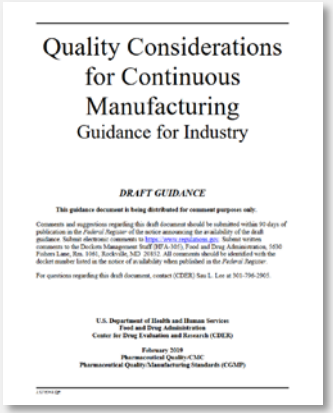
Emerging Technology Program

- Supports industry's development and implementation of innovative approaches in **pharmaceutical design and manufacturing**
- Identifies and **resolves potential scientific and policy issues** related to new approaches
  - Enabled the first switch from batch to continuous manufacturing (CM) for an approved drug
- A website and Guidance for Industry are posted



Emerging Technologies for…

- **Small molecules**


Quality Considerations for Continuous Manufacturing
Guidance for Industry

DRAFT GUIDANCE

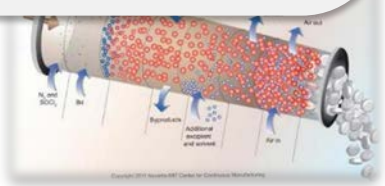
This guidance document is being distributed for comment purposes only.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

February 2019
Pharmaceutical Quality/CMC
Pharmaceutical Quality/Manufacturing Standards (CGMP)

New Draft Guidance on Quality Considerations for Continuous Manufacturing

for aseptic filling, novel container and closure systems for injectable products



Pre-ANDA Program

Complex Products

COMPLEX…	Example	Products
Active ingredients	Peptides, complex mixtures, natural source products	Glatiramer acetate
Formulations	Liposomes, emulsions	Liposomal formulations
Routes of Delivery	Locally acting drugs such as dermatological products and complex ophthalmological products	Acyclovir cream
Dosage Forms	Transdermal systems, extended release injectables	PLGA microspheres
Drug-Device Combinations	Dry powder inhalers, nasal sprays, transdermal systems	Mometasone nasal spray
Other products	Complexity or uncertainty concerning the approval pathway that would benefit from early scientific engagement	Abuse deterrent opioid formulations

Pre-ANDA Program for Complex Products

- **Clarifies regulatory expectations for prospective applicants early in product development**
  - Product Development Meetings
- **Assists applicants in developing more complete submissions**
  - Pre-Submission Meetings
- **Promotes a more efficient and effective assessment process reducing the number of cycles to approval**
  - Mid-Review Cycle Meetings

Innovative Approaches to Quality Assessment

Challenges with Current State

The quality assessment is a freestyle narrative:

- Unstructured text
- Summarization of application information
- “Copy and paste” data tables

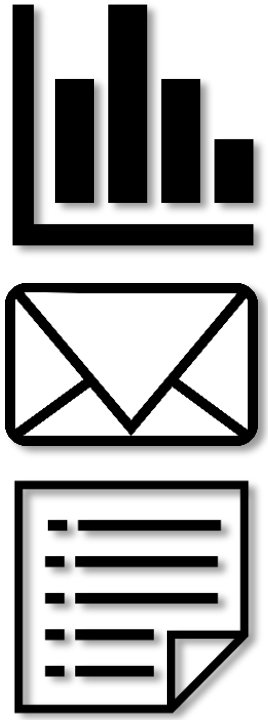
Encumbers best practices for:

- Knowledge sharing
- Managing quality across the product lifecycle
- Overall modernization

KASA:
Knowledge-aided Assessment & Structured Application

An FDA initiative to:

- Enhance submission format to allow automated tools
- Establish algorithms for risk identification, mitigation, communication, and comparison
- Provide a structured assessment that eliminates unnecessary tasks and narratives
- Capture and manage knowledge over the lifecycle of drug products

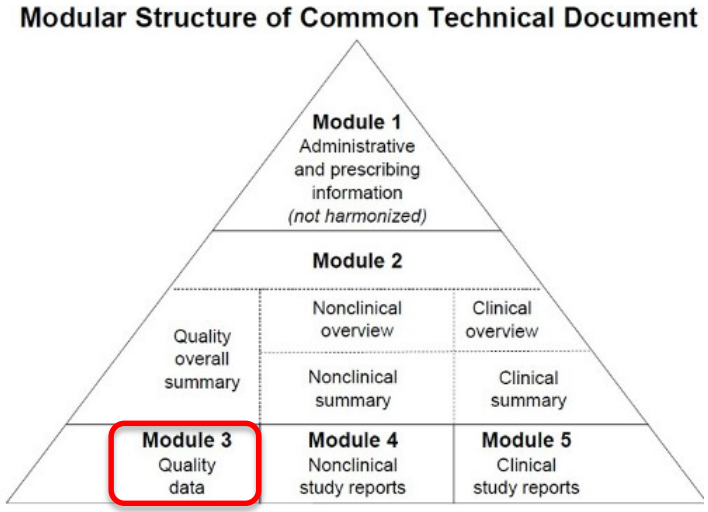


PQ/CMC

Product Quality/Chemistry, Manufacturing, and Control

An FDA initiative to:

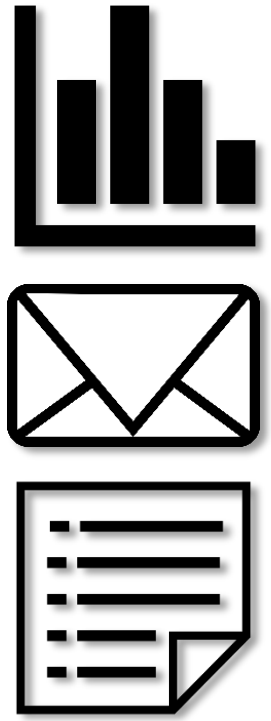
- Identify and prioritize eCTD Quality sections amenable to a structured approach
- Provide recommendations for data standardization to facilitate application assessment and quality data management (i.e., KASA)



KASA and PQ/CMC Together:

Benefits to the FDA:

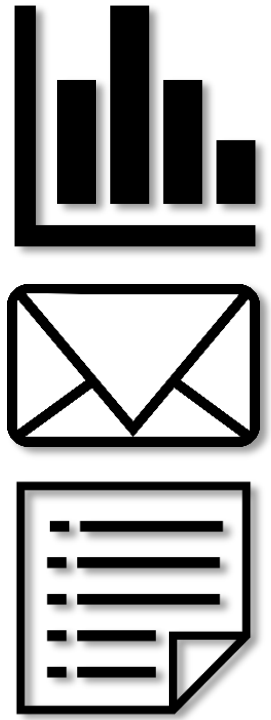
- Enhances consistency and objectivity of regulatory assessment
- Enables knowledge management of product, manufacturing, and facility
- Accelerates regulatory action and decision-making



KASA and PQ/CMC Together:

Benefits to industry and patients:

- Clearer regulatory expectations
- Increased 1st cycle approvals (esp. generics)
- More affordable and accessible medicines




Pharmaceutical quality is attained through commitment, investment and partnership


FDA
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