

Advancing Drug Product Quality

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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.

A close-up photograph showing a hand holding an orange pill bottle, pouring white, oval-shaped pills into the palm of another hand. The background is blurred, focusing attention on the action of dispensing medication.

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

A close-up photograph of a person's hands. The left hand holds an orange plastic pill bottle, tilted to pour white, oval-shaped pills into the palm of the right hand. The background is softly blurred, focusing attention on the action of dispensing medication.

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

A close-up photograph showing a person's hand holding an orange plastic pill bottle. The bottle is tilted, and several white, oval-shaped pills are falling from its opening into the palm of another hand held below it. The background is softly blurred, focusing attention on the action of dispensing the medication. A white label with a yellow section is partially visible on the side of the bottle.

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

Pharmaceutical Quality Oversight



~~Across all drug classes...~~

new drugs

compounded
drugs

biologics

over-the-counter
drugs

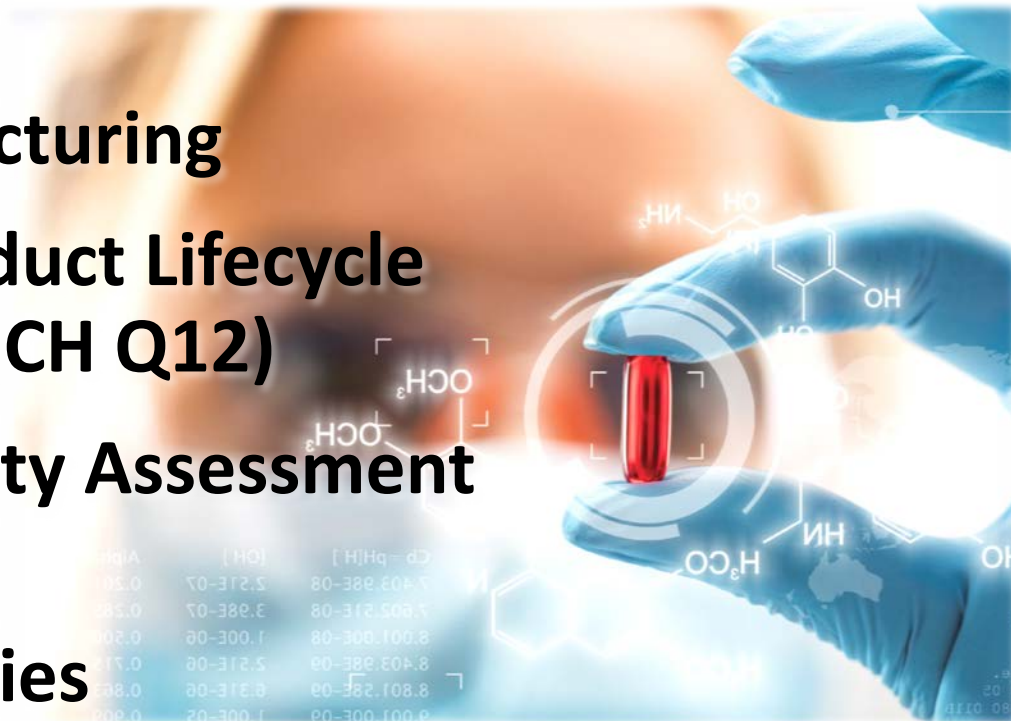
generics

biosimilars



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**

A close-up photograph showing a hand holding an orange plastic pill bottle. The bottle is tilted, and several white, oval-shaped pills are falling from its opening into the palm of another hand held below it. The background is softly blurred, focusing attention on the action of dispensing the medication. A white label with a yellow section is partially visible on the bottle, though the text is mostly obscured or illegible.

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

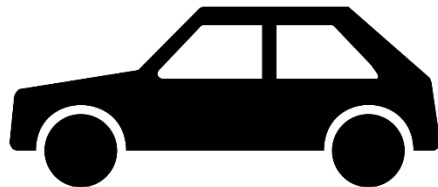
- [Product Quality/Chemistry Manufacturing and Control \(PQ/CMC\)](#)

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

Center for Drug Evaluation and Research

CDER Offices and Divisions

Drug Safety Oversight Board

Jobs at the Center for Drug Evaluation and Research (CDER)

Meeting Presentations (Drugs)

CDER Exclusivity Board

FAQs about CDER

Reports & Budgets (CDER)

Manual of Policies & Procedures (CDER)

Contact CDER

Emerging Technology Program

Background

CDER's Office of Pharmaceutical Quality created the Emerging Technology Program (FDA Voice on Modernizing Pharmaceutical Manufacturing to Improve Drug Quality: Ensuring a Safe and Adequate Supply of Drugs) to promote the adoption of innovative approaches to pharmaceutical product design and manufacturing. The program leverages existing resources within the Agency to facilitate the regulatory quality assessment (including both review and inspection) of submissions to the Agency involving novel technologies likely to improve product safety, identity, strength, quality, and purity. The program features the Emerging Technology Team (ETT), which includes representation from all FDA pharmaceutical quality functions, to provide cross-functional expertise to the questions posed by program participants on their proposed technology.

About the Emerging Technology Program

Emerging Technology Program

Emerging Technology Program

Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
September 2017
Pharmaceutical Quality/CMC

CDER 2017

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.

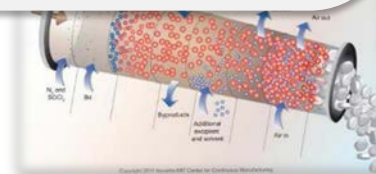
Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the Federal Register of the notice announcing the availability of the final guidance. Submit electronic comments to <https://www.fda.gov/oc/ohrt>. Submit written comments to the Division of Regulatory Operations, Office of Regulatory Affairs, Food and Drug Administration, 1015 Fishers Lane, Room 1041, Rockville, MD 20852. All comments should be identified with the document number listed in the notice of availability when published in the Federal Register. For questions regarding this draft document, contact CDER, via L. Lee at 301-796-2963.

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

February 2018
Pharmaceutical Quality (CMA)
Pharmaceutical Quality Manufacturing Standards (PQMS)

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



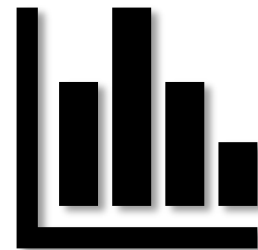
Encumbers best practices for:

- 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

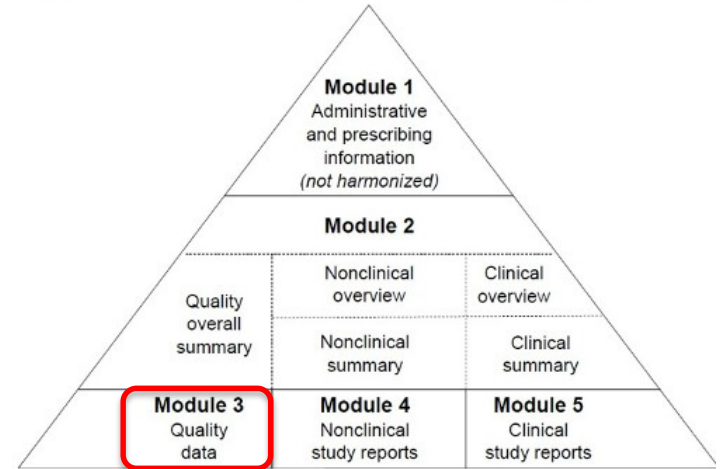


Product Quality/Chemistry, Manufacturing, and Control

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)

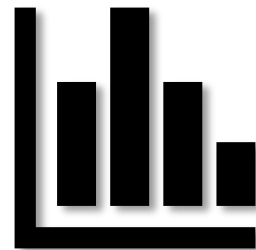
Modular Structure of Common Technical Document



KASA and PQ/CMC Together:

Benefits to the FDA:

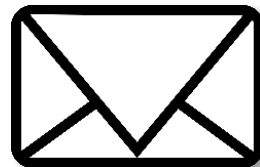
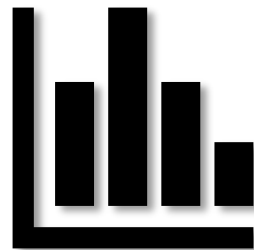
- Enhances consistency and objectivity of regulatory assessment
- Enables knowledge management of product, manufacturing, and facility
- Accelerates regulatory action and decision-making



KASA and PQ/CMC Together:

Benefits to industry and patients:

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



A close-up photograph showing a hand holding an orange pill bottle, pouring white, oval-shaped pills into the palm of another hand. The background is softly blurred, focusing attention on the action of dispensing medication. The text is overlaid on the left side of the image.

**Pharmaceutical quality is attained
through commitment, investment
and partnership**



U.S. FOOD & DRUG
ADMINISTRATION