Overview of Policy Document Options, Development, and Oversight

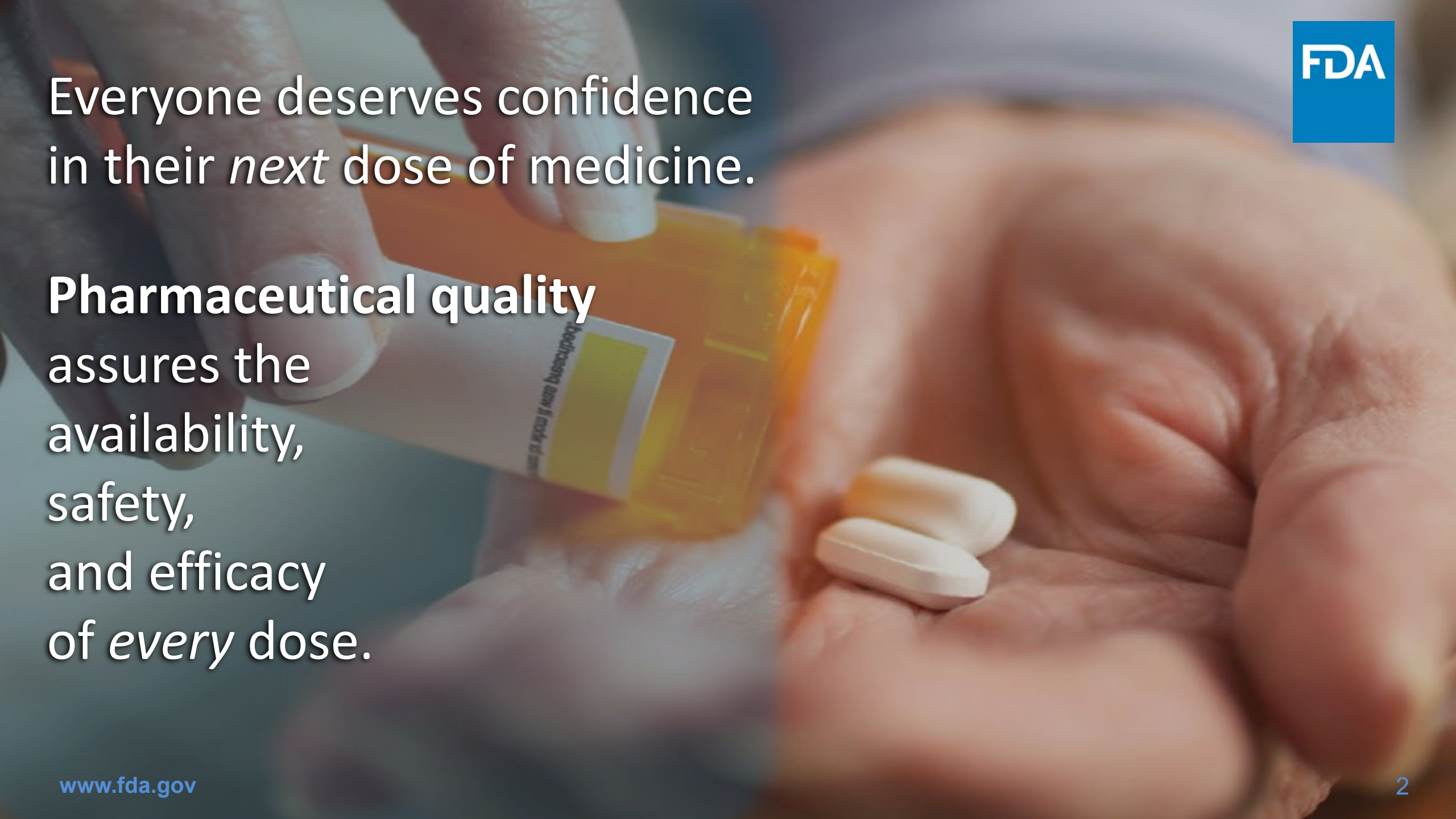
Leila Wieser

Director, Editorial and Project Management Staff

OPPQ| OPQ | CDER | FDA

Pharmaceutical Quality Symposium 2023: Quality, Supply Chain & Advanced Manufacturing

October 31, 2023



Everyone deserves confidence in their *next* dose of medicine.

Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

Outline

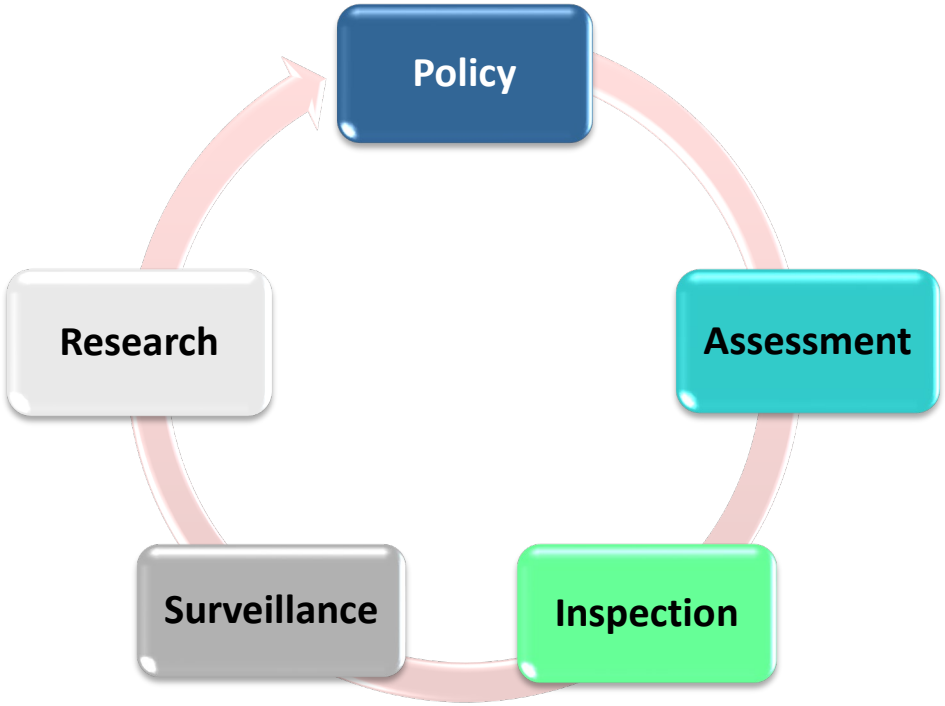
1. Introduction to OPPQ
2. Examples of Policy Documents OPPQ Manages
3. Policy Development Process
4. Understanding the Regulatory Framework
5. How to Engage with OPPQ

Why OPPQ?

- Policy offices exist throughout the other CDER offices
- Different approaches to policy-setting in different offices
- Office of Policy for Pharmaceutical Quality (OPPQ) created to have a dedicated office with dedicated staff, focused exclusively on pharmaceutical quality
- Pharmaceutical quality is a topic that touches all products regulated by CDER and CBER
- Pharmaceutical quality touches all UFA programs (GDUFA, BsUFA, PDUFA, and OMUFA)

Examples of OPPQ Work Products

- Regulations
- Guidances
- Manual of Policies and Procedures (MAPPs)
- Compliance Programs
- Memorandum of Understanding (MOUs)
- Staff Manual Guides (SMGs)
- Citizen Petition consults/responses
- Controlled correspondence
- External inquiries (NDA/BLA/CGMP/503B compounding)
- USP inquiries/PF review
- Media inquiries
- Legislative inquiries (TA, Congressional inquiries, GAO, OIG)
- Individual policy questions/issues
- Evaluation of existing policy documents
- Informal standards recognition program
- Request for Reconsideration, Formal Dispute Resolutions, Forfeiture Analysis



Guidance for Industry

See https://www.fda.gov/regulatory-information/search-fda-guidance-documents to search guidances

What Is a Guidance?

Guidances assist industry in carrying out its obligations under laws and regulations on subjects such as the content and submission of applications and the design, production, manufacturing, and testing of regulated products.

What Is a Guidance? (cont.)

- Level 1 guidances provide FDA's initial interpretations of new or revised significant regulatory requirements, while Level 2 guidances usually address existing practices or minor changes in FDA's interpretation or policy

- Draft guidances describe new or significantly changed policy, are published for public comment through a public docket, and are not for implementation, while final guidances incorporate those public comments provided after a draft or revised draft has been published, are considered FDA's current thinking, and are for implementation

Non-Binding vs. Binding Guidance

- FDA guidance documents are generally non-binding

"This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page."

- In rare cases, where Congress has given FDA the authority to issue a binding guidance, we can issue partially or fully binding guidances. The guidance would include "binding" language.
- As an example, the guidance on "Comparability Protocols for Postapproval Changes to the Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA" has both binding and nonbinding language https://www.fda.gov/regulatory-information/search-fda-guidance-documents/comparability-protocols-postapproval-changes-chemistry-manufacturing-and-controls-information-nda.

Manual of Policies and Procedures (MAPPs)

See https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp to search MAPPs

What Is a MAPP?

- Policies and procedures primarily intended to direct CDER staff in the conduct of their work (directives) may be published in a CDER MAPP (Manual of Policies and Procedures). A MAPP serves to disseminate the policies and procedures.
- Most MAPPs are posted for public view for the purpose of transparency; however, unlike guidance to industry, MAPPs are not intended to provide guidance to or gain public comment from the regulated industry.

MAPP Categories and Review

- Standard, interim, and internal MAPPs: Intended for either internal or external audiences, depending on their content
- Review Cycles: MAPPs have periodic review cycles to ensure continued relevance and effectiveness

Compliance Programs

See https://www.fda.gov/drugs/guidance-compliance-regulatory-information/drug-compliance-programs to search Compliance Programs

What is a Compliance Program?

FDA's Compliance Programs provide instructions to FDA personnel for conducting activities to evaluate industry compliance with the Federal Food, Drug, and Cosmetic Act and other laws administered by FDA.

Policy Document Lifecycle in OPQ

1. Prioritization: Consider Statutory/UFA/Public Health Emergency/Agency/Center priorities
2. Working Group: Policy writing/development
3. Clearance
4. Publication
5. Implementation (e.g., training, communication)
6. Policy Document Review: Periodic review to ensure continued relevance and effectiveness

Understanding the Regulatory Framework

- Regulations lay out policy requirements at a very high level (e.g., not every testing method discussed)
- Guidance to Industry provides FDA's interpretation of the statute and regulations to provide recommendations on specific topics (e.g., extractables/leachables)
- MAPPs and Compliance Programs internally operationalize what we have stated in guidance and regulations

Read these together to better understand FDA requirements and recommendations!

Using FDA's Policy Documents – example 1

TOPIC: Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products

- Guidance for Industry: Describes recommendations for industry to comply with 21 CFR 201.51(g) for injectable (liquid, solids for reconstitution) drugs while mitigating inappropriate excess volume
  - Clarifies the FDA regulatory requirements and recommendations pertaining to allowable excess volume in injectable vials and describes when justification is needed for a proposed excess volume in these injectable drug products.
  - Discusses the importance of appropriate fill volumes for injectable drug products and recommends that labeled vial fill sizes be appropriate for the intended use and dosing of the drug product.
  - https://www.fda.gov/media/88138/download

Use the guidance to understand the relevant regulatory framework (e.g., applicable regulations) and FDA's recommendations on how to address this issue in your application

Using FDA's Policy Documents – example 1

TOPIC: Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products

- MAPP 5019.1 Rev 1: Describes how CDER OPQ will consistently assess fill volume for injectable (liquid, solids for reconstitution) drugs
  - Describes the policies and procedures for product quality assessors to ensure consistent assessment of excess volumes in injectable drug products packaged into vials.
  - Addresses liquid, as well as solid, drug products that require reconstitution/constitution.
  - Describes the policies and procedures to be used by OPQ product quality assessors to ensure the excess injectable drug product is sufficient to allow for withdrawal and administration of the net container content of the drug product.
  - https://www.fda.gov/media/155066/download?attachment

Read the MAPP to understand what OPQ assessors will be looking for in your application; use this to double check your understanding of the guidance

Using FDA's Policy Documents – example 2

TOPIC: Process Validation for Drug Manufacturing

- Statute and Regulations relevant to process validation:
  - 501(a)(2)(B) of the FD&C Act: Provides that a drug shall be deemed adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.
  - 21 CFR 211.100(a) and 211.110(a): CGMP regulations for validating drug manufacturing require that drug products be produced with a high degree of assurance of meeting all the attributes they are intended to possess.

See these relevant provisions of FDA's statutory and regulatory authority to understand the relevant requirements

Using FDA's Policy Documents – example 2

TOPIC: Process Validation for Drug Manufacturing

- Guidance for Industry: Process Validation: General Principles and Practices (January 2011)
  - Outlines general principles and approaches that FDA considers to be appropriate elements of process validation for drug and biological products, including active pharmaceutical ingredients (APIs or drug substances).
  - Incorporates principles and approaches that all manufacturers can use to validate manufacturing processes.
  - Aligns process validation activities with the product lifecycle concept and relevant ICH guidances.
  - https://www.fda.gov/files/drugs/published/Process-Validation--General-Principles-and-Practices.pdf

Use the guidance to understand more fully how to design and implement process validation activities

Using FDA's Policy Documents – example 2

- Compliance Program: 7356.843 Postapproval Inspections
  - Describes how FDA will assess, among other objectives, CGMP compliance regarding process validation lifecycle activities for approved drugs.
  - Provides risk-based strategies for the scope of inspectional coverage and clarifies roles to establish efficient communication.
  - https://cacmap.fda.gov/media/164791/download

Read the compliance program to understand what process validation information FDA investigators may evaluate when inspecting your manufacturing facility

Final Thoughts

- Remember:
  - When you're looking at a draft or finalized guidance, also look for related MAPPs and Compliance Programs to provide further insight into the guidance
  - MAPPs and Compliance Programs are how FDA operationalizes our interpretation of a rule or regulation, so they will help greatly with understanding FDA's practices and how FDA ensures consistency
  - These policies are intended to be understood and used to ensure our goal of safe, effective, quality products

How to Engage with OPPQ

- Send any questions or comments you have to:
  - CDER-OPQ-Inquiries@fda.hhs.gov

THANK YOU!

For this opportunity to strengthen our partnership with you!