FDA Update

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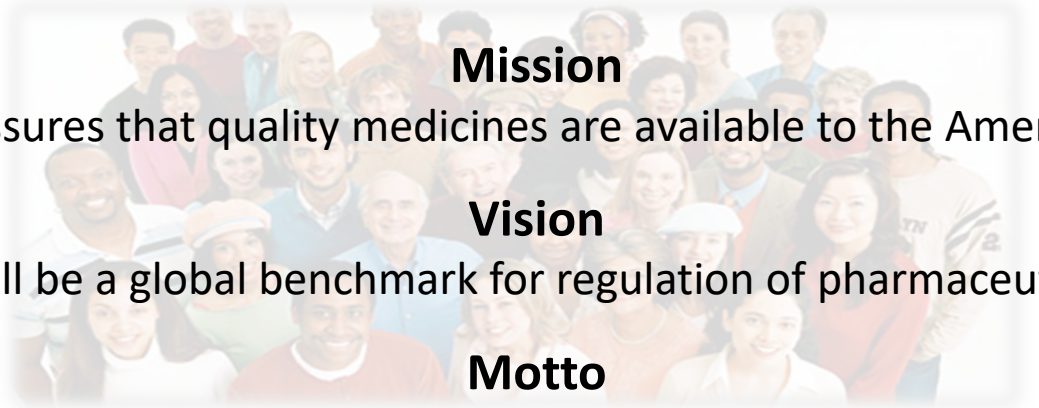
CDER/OPQ

Office of Pharmaceutical Quality

Pharmaceutical quality is our *shared* goal of assuring consistently safe and effective drugs are available to patients and consumers.

Pharmaceutical quality is what gives them confidence in their *next* dose.



Mission

OPQ assures that quality medicines are available to the American public

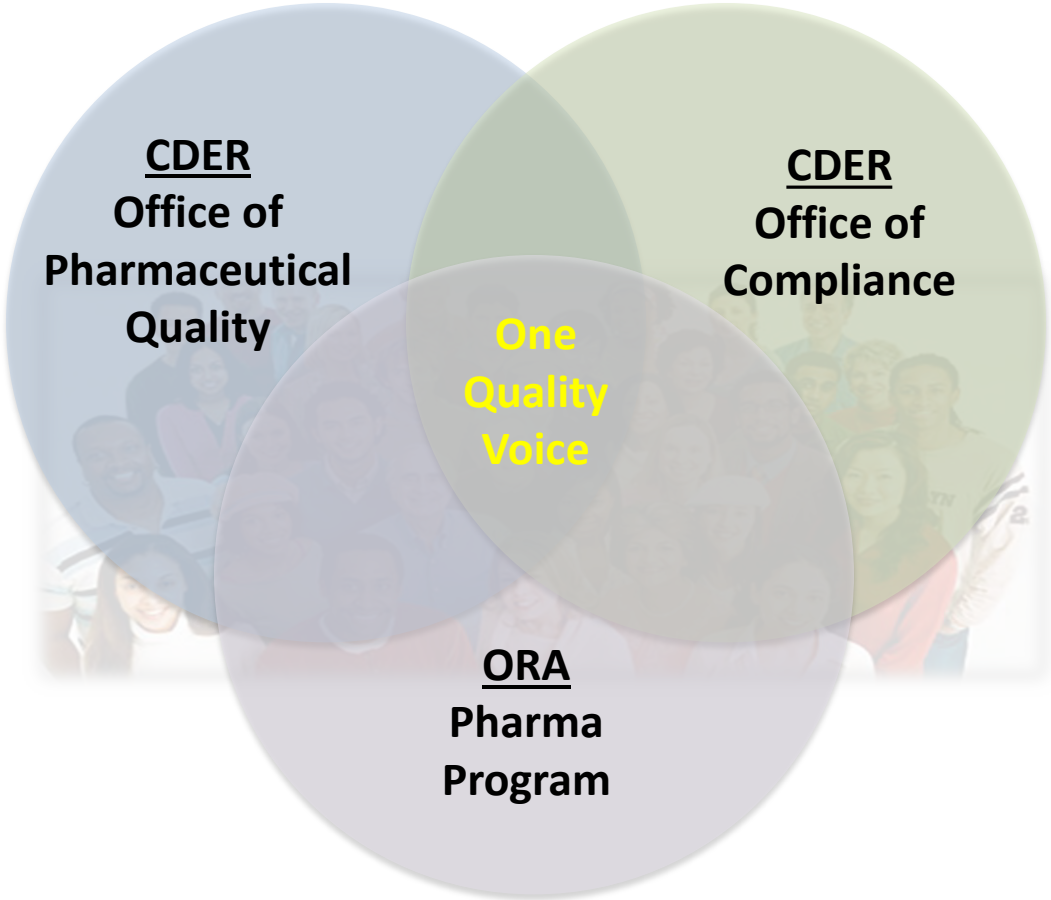
Vision

OPQ will be a global benchmark for regulation of pharmaceutical quality

Motto

One Quality Voice

One Quality Voice

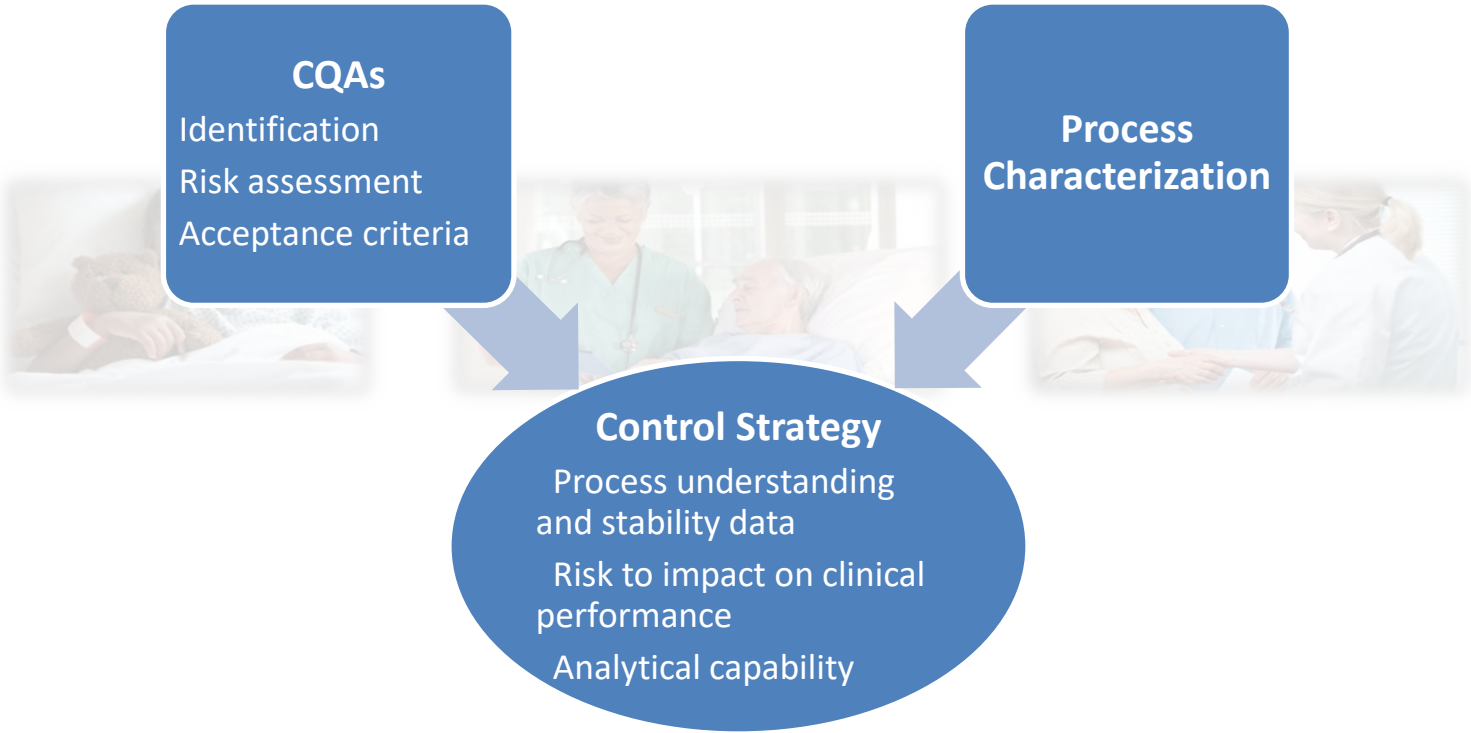


Patient-Focused Quality Standards

- Product quality is the foundation upon which the clinical safety and efficacy assessment rests
- A product is “fit for use” if it meets the established quality attributes
  - Purity, potency/strength, identity, bioavailability/delivery, labeling/packaging, performance, etc.
- Strive to establish *Quality Standards* using appropriate correlations between quality attributes and clinical performance
  - Linking quality to clinical performance helps to assure that drug product will perform as indicated in the label
- Emphasize specifications that relate process capability to clinical relevance

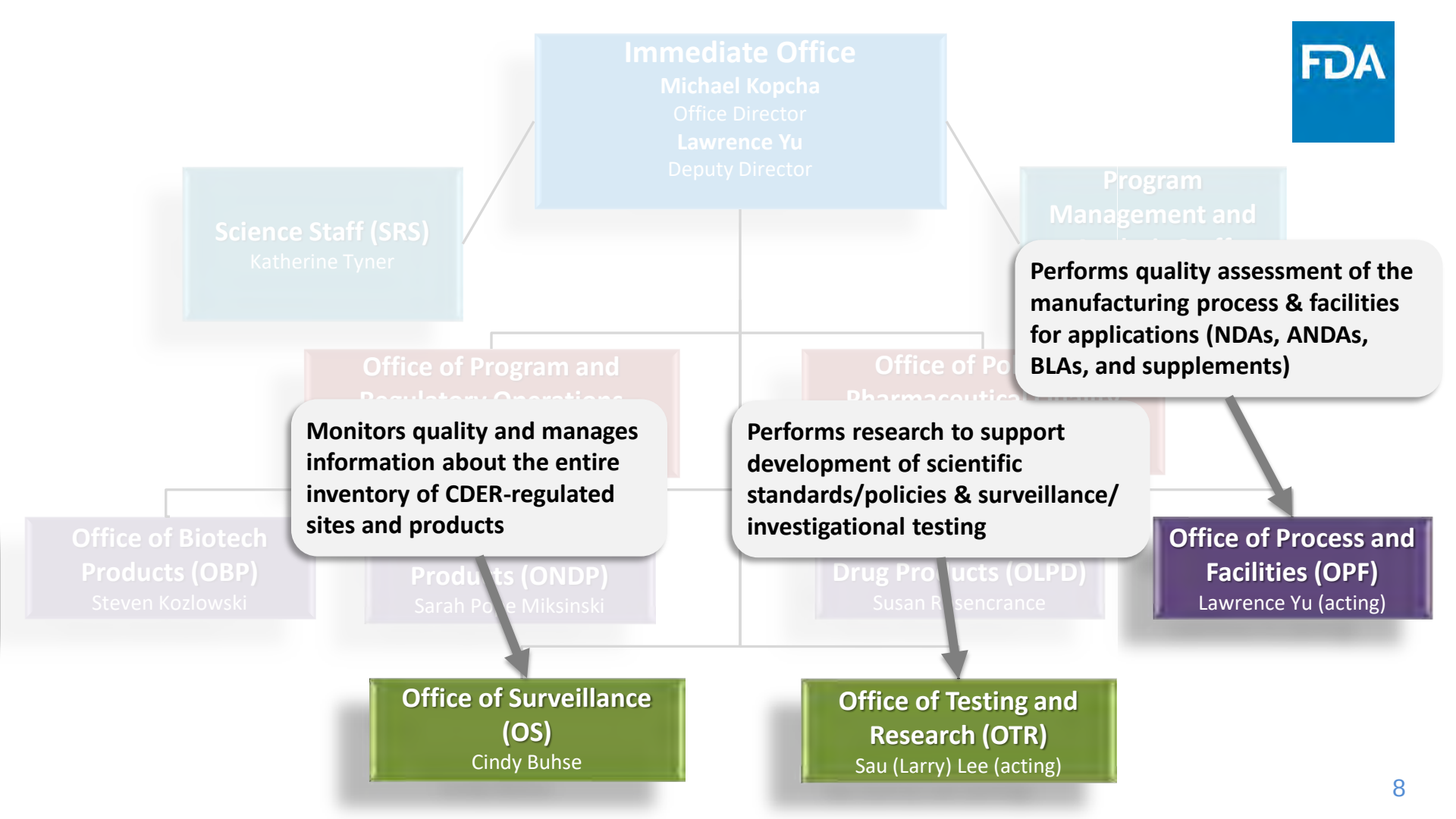
Patient Focus and Control Strategy

- Manufacturers should pursue development of a patient-focused, risk-based, overall control strategy



OPQ Organization Updates

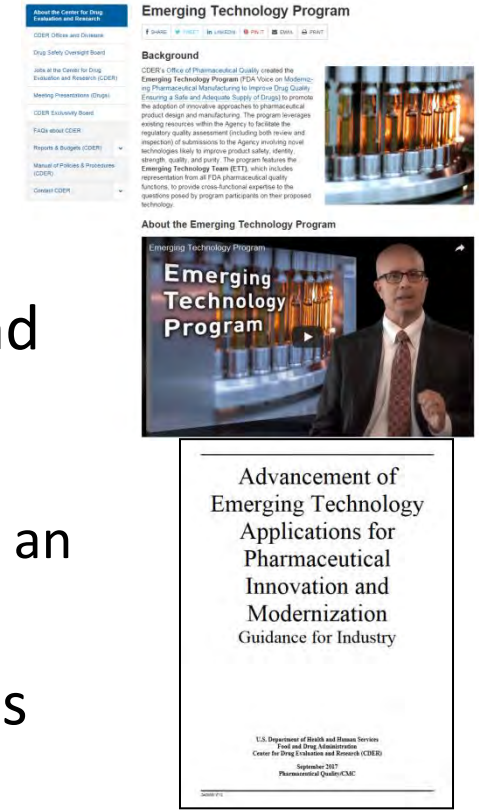
Office of Pharmaceutical Quality


Immediate Office
Michael Kopcha
Office Director
Lawrence Yu
Deputy Director
Science Staff (SRS)
Katherine Tyner
Program Management and
Performs quality assessment of the manufacturing process & facilities for applications (NDAs, ANDAs, BLAs, and supplements)
Office of Program and
Monitors quality and manages information about the entire inventory of CDER-regulated sites and products
Performs research to support development of scientific standards/policies & surveillance/ investigational testing
Office of Biotech Products (OBP)
Steven Kozlowski
Office of Process and Facilities (OPF)
Lawrence Yu (acting)
Office of Surveillance (OS)
Cindy Buhse
Office of Testing and Research (OTR)
Sau (Larry) Lee (acting)

Promoting innovation and availability of quality drugs

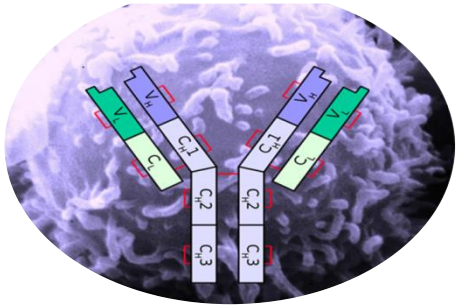
Emerging Technology Program

- 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 approval of the first switch from batch to continuous manufacturing process for an approved drug
- A new website and Guidance for Industry has posted



OPQ Science and Research

Immunology

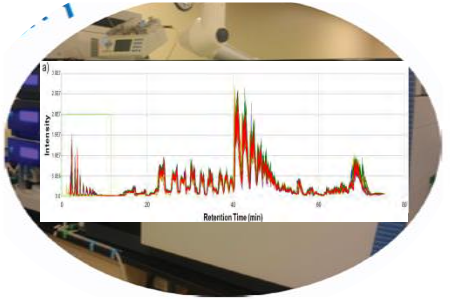


Manufacturing Science & Innovation

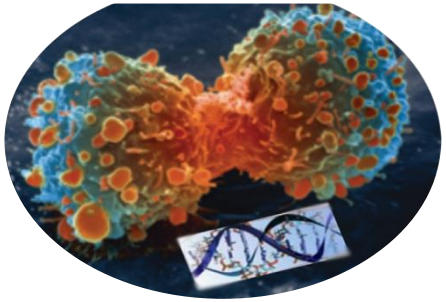
Manufacturing and Controls for Small Molecule Drugs

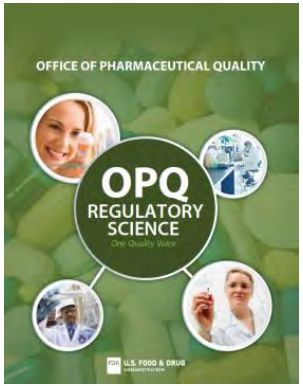
Manufacturing and Controls for Biological Products

Pharmaceutical Analysis & Characterization

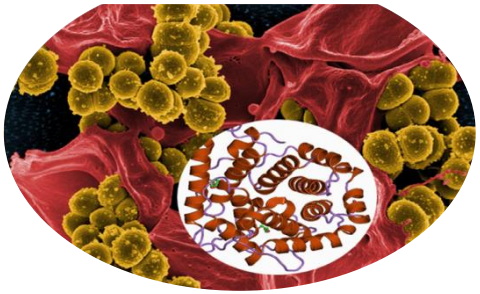


Tumor Biology





Infectious Disease & Inflammation



Internal and External Collaboration

External Collaboration

- U.S. Pharmacopeial Convention (USP)
- ASTM International (ASTM)
- The Pharmaceutical Research and Manufacturers of America (PhRMA)
- Association for Accessible Medicines (AAM) [formerly Generic Pharmaceutical Association (GPhA)]
- Biotechnology Industry Organization (BIO)
- International Pharmaceutical Excipients Council (IPEC)
- American Association of Pharmaceutical Scientists (AAPS)
- Personal Care Products Council (PCPC)
- International Society for Pharmaceutical Engineering (ISPE)
- Parenteral Drug Association (PDA)
- Product Quality Research Institute (PQRI)
- US National Institute of Standards and Technology (NIST)
- Bulk Pharmaceutical Task Force (BPTF)
- Drug Information Association (DIA)
- Pharma and Biopharma Outsourcing Association (PBOA)
- International Forum on Process Analytical Chemistry (IFPAC)

CDER's Current Standards Engagement

- **USP**
  - USP Committees
    - **Chemical Medicines**
    - **Nomenclature and Labeling**
    - **Compounding**
    - **Excipients**
    - **General Chapters (Chemical & Physical Analysis, Dosage Forms, Statistics, Microbiology, Packaging, Storage and Distribution)**
  - Harmonization between USP, EP, JP through the Pharmacopeial Discussion Group
- **ASTM E55** Manufacturing of Pharmaceutical and Biopharmaceutical Products, **D10** Packaging, **E11** Statistics, **56** Nanotechnology
- **ISO Activities** - Combination Product Standards (pre-filled syringes, device change management), **ISO TC 229** Nanotechnologies**, ISO TC 217 WG 7** (sunscreens)

FDA-USP Collaboration

- FDA (CDER, CBER, CDRH, CVM, CFSAN) has over 100 liaisons to USP Expert Committees and Expert Panels
- FDA and USP management hold quarterly meetings to discuss direction and provide bidirectional feedback
- FDA supports monograph modernization, including updates to OTC monographs
- FDA-USP-CHPA roundtable in September 2017
  - Brainstormed various potential approaches to developing USP quality standards for non-application OTC products
  - Working with OND, OC, and ORA to achieve consensus on regulatory issues

FDA-USP Collaboration

- ORISE projects (OTR/DPA, OTR/DPQR, and ORA NY-DO)
  - Assay and Impurity Methods for Diphenhydramine and Phenylephrine Hydrochloride Tablets
  - Assay and Organic Impurity Analysis for Diphenhydramine HCl Powder
  - Glass packaging standards
  - Evaluation of Circular Dichroism as a technique to detect and quantify chiral impurities
- CRADA projects with ORA
  - Items on Monograph Modernization priority list
  - FDA provided input based on survey of CDER, CVM, and ORA staff
- Monthly meetings
  - Progress of lab projects
  - Nomenclature issues: Multi-ingredient products, unique dosage forms

Proposed Approach for the Use of Standards

- Development of a CDER informal standards recognition program is under consideration
- Benefits to FDA and Industry would include:
  - Providing industry with useful reference materials/guidance
  - Review effort can be more focused
- Promotes transparency/accountability in the development of standards
- Complements OPQ's other policy development efforts

Proposed Approach for CDER

- Publish Notice of Intent re: 'Informal' recognition/non-binding standards program
  - statement of policy vs. substantive rule
- Publish guidance on details of the program
  - Different from CDRH standards recognition program, which was created as a result of FDAMA of 1997
    - CDRH standards recognition program requires Notice & Comment
- Allow anyone (internal or external) to propose/submit a standard for recognition with relevant information
- Ability to informally recognize a standard in whole or in part
- CDER would develop a mechanism to review and publish 'Information Sheet' on website describing scope and other relevant information for each recognized standard

Other Considerations/Next Steps

- Develop a process that is fair, unbiased, and transparent
  - How to evaluate requests for recognition
  - Criteria for evaluation of SDO and standard
- Guidance and associated Q&A to explain the process and how the program will work
  - Description of program
  - Qualifying criteria and exclusion criteria
  - Procedures to informally recognize a standard
  - Procedure for posting/updating CDER website

International Collaboration Initiative

- Enhances mutual understanding of the quality assessment processes and practices in global regulatory agencies
- Identifies best practices in foreign regulatory agencies to enhance efficiency of our assessment processes
- Sets a foundation for future collaboration among agencies
- Technical experts from OPQ are analyzing potential ways to increase the efficiency of quality assessment processes and practices, based on visits with:
  - Australian Therapeutic Goods Administration (TGA)
  - Japan's Pharmaceutical and Medical Device Administration (PMDA)
  - European Medicines Agency (EMA)
  - Health Canada

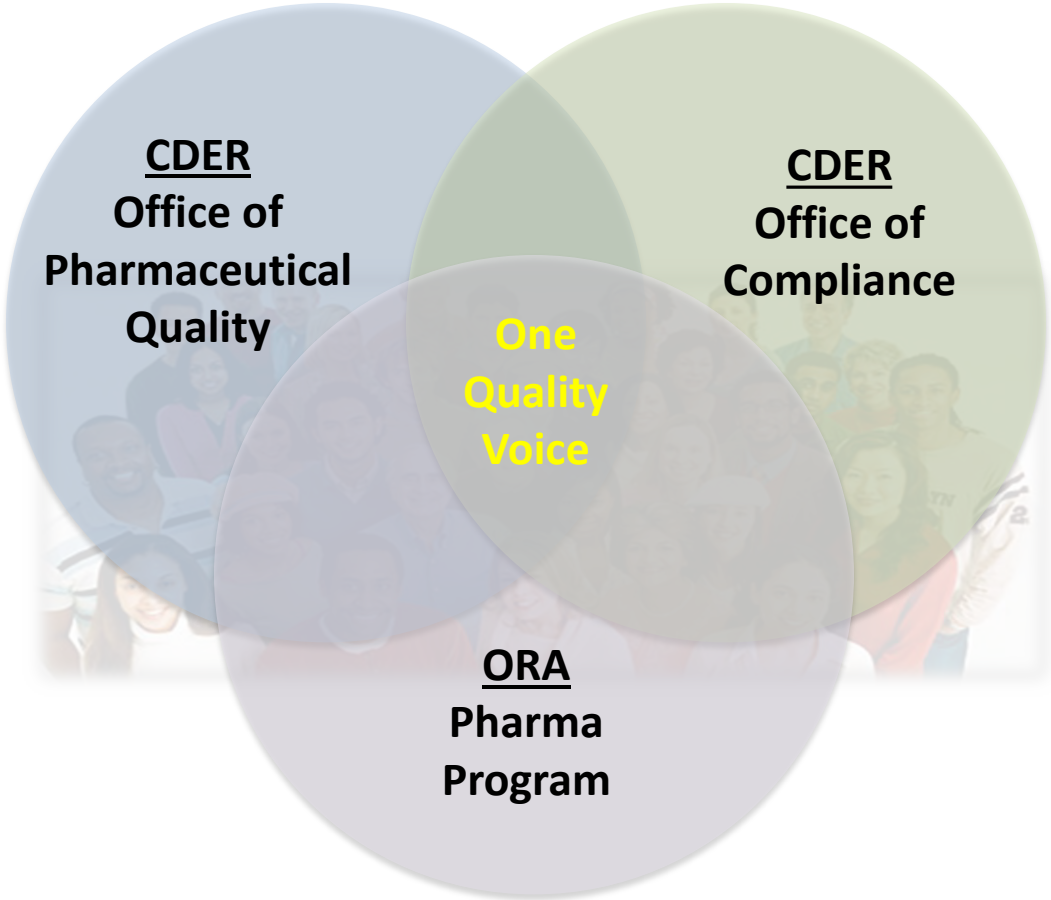
Other International Harmonization Efforts

- PIC/S
  - Development of aide memoires to harmonize inspections; participation on expert circles and training efforts
  - Relationships with many regulators; sharing of timely quality information (e.g., product quality defects, recalls)
- ICH
  - Q12 “Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management”
  - M9 “Biopharmaceutics Classification Based Biowaivers”
- WHO

Mutual Recognition Agreement with EU

- Purpose:
  - Facilitate “exchange of official GMPs documents” and “reliance on the factual findings....”
  - “Facilitate trade and benefit public health” by being more efficient at inspections
- Implementation begins Nov. 1, 2017 if…
  - EU completes assessment of FDA and FDA completes assessments of at least 8 Member States
- Includes the vast majority of drugs
  - All CDER-covered products
- Certain products will be reevaluated in the future, such as vaccines and veterinary products
- Either party may ask the other to perform pre-approval inspections of marketed human drug facilities located within the US or EU

Internal Collaboration



Concept of Operations for Facility Evaluations and Inspections

- Signed in Summer 2017, a collaboration between ORA, OC, and OPQ
  - Outlines the workflow processes for **Pre-Approval**, **Post-Approval**, **Surveillance**, and **For-Cause** Inspections
  - Defined and clarified the roles and responsibilities of CDER and ORA
- Ensures **consistency, efficiency, and transparency** in facility evaluations, inspections, and regulatory decision-making for marketing applications
- Improves **strategic alignment** and **operational capacity** by enhancing collaboration across CDER and ORA

ConOps Highlights

- CDER and ORA are currently working to begin implementation of the ConOps in the fall of 2017
- Includes a commitment to communicate Surveillance Inspection final classifications to facility owners within 90 days of the end of an inspection (90% of the time)
- There will be updates to related documents such as:
  - Manuals of Policies and Procedures (MAPPs)
  - Compliance Program Guidance Manuals (CPGMs)
  - Investigations Operations Manual (IOM)
  - Regulatory Procedures Manual (RPM)

New Inspection Protocol Project

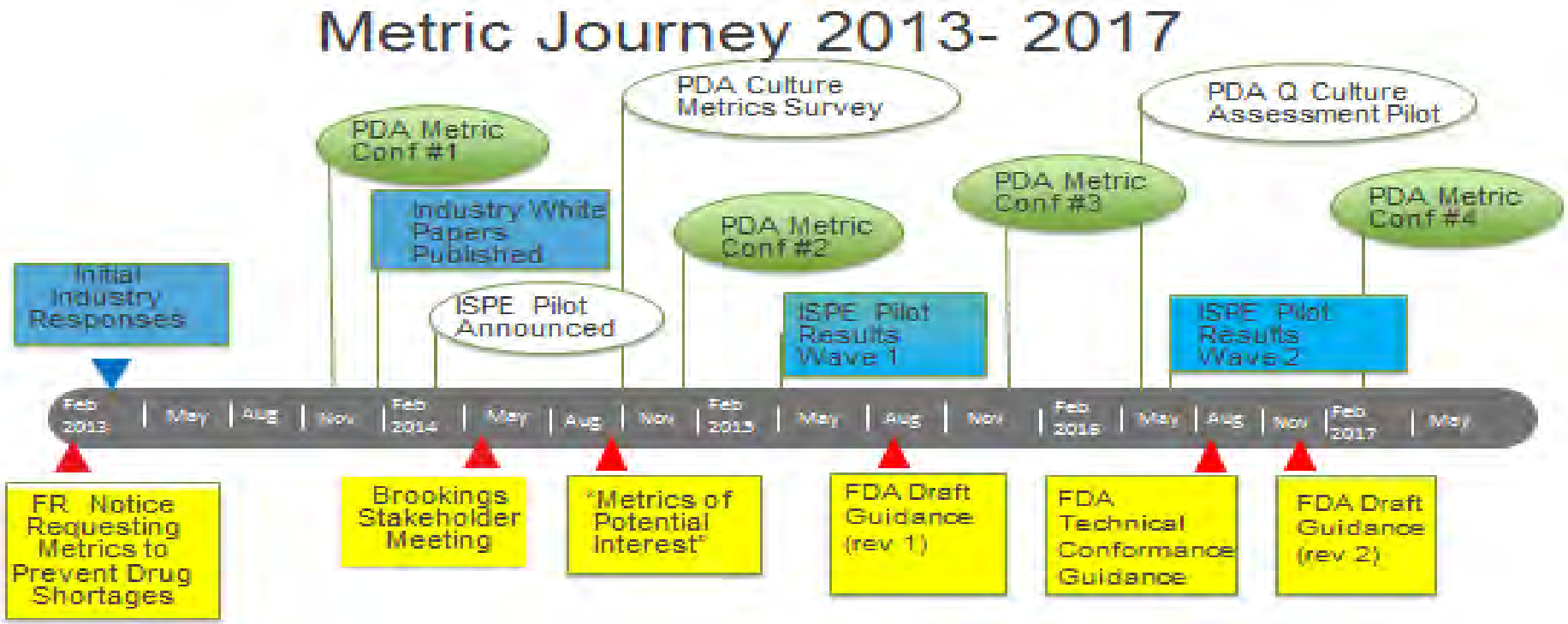
- In 2014, FDA proposed a new paradigm for more efficient and effective inspection and reporting
- The Office of Pharmaceutical Quality (OPQ), the Office of Regulatory Affairs (ORA), and the Office of Compliance (OC) established a Steering Committee to develop and implement NIPP
- Goals include:
  - A streamlined approach for Pre-Approval and Surveillance Inspections that provides organized reporting to facilities through application of **standardized inspection protocols** and **templated/semi-automated inspection reports**
  - **A consistent, objective approach for assessing a facility's state of quality** during Pre-Approval and Surveillance Inspections to inform facility owners and enable them to improve quality

OPQ Policy Efforts

Quality Policy Activities in 2017

- Published **7 MAPP documents**
- Responded to **220 external inquiries**
- Responded to **371 controlled correspondence**
- Published **7 guidance documents**
  - ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications
  - Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization (Final)
  - CMC Post-approval Manufacturing Changes for Specified Biological Products To Be Documented in Annual Reports
  - Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products
  - Child-Resistant Packaging Statements in Drug Product Labeling
  - Current Good Manufacturing Practice for Medical Gases
  - Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles

Quality Metrics Program



Public Comments on Revised Draft Guidance

26 Comments Received to the 2016 Revised Draft (vs. 80 for 2015)

- Trade associations
- Individual companies
- Contract manufacturers
- OTC industry
- Academics
- Manufacturers of APIs, atypical APIs, excipients
- Purchasers

Key Messages from Stakeholders

- Desire for FDA to make a stronger link to the value and utility of the data and describe how we intend to measure success of the program
- Hate the list but want to be at the table
  - Incentives need to be strengthened – reporters list not viewed as an incentive
  - Industry finds direct collaboration with FDA a strong incentive
- Start with a pilot with industry input
- Definitions still a challenge
  - Collaborate with industry to set definitions
  - Some recognize a value to industry in having consistent definitions
  - Some recommend to only collect metrics across a single company to reduce need to develop common definitions across industry

What's Next?

- Quality metrics remains important to FDA
  - Encourage firms to refine an existing program or initiate a new program as an important step toward building a quality culture
- FDA is continuing to engage with industry in a listening mode – we want to understand industry concerns and suggestions for how to move the program forward
- Portal development near completion – we still plan to request voluntary testing using dummy data
- More to come…

In Closing…

OPQ

- Is committed to:
  - Patient-focused quality standards
  - Strengthening our internal and external collaborations to better assure the availability of quality drugs
  - Ongoing participation in global harmonization efforts to reduce barriers to innovation and continual improvement in manufacturing
  - Partnering with stakeholders to increase appreciation for the importance of quality

Thank You!!

CDER-OPQ-Inquiries@fda.hhs.gov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