Regulation of Pharmaceutical Quality in the US

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Learning Objectives

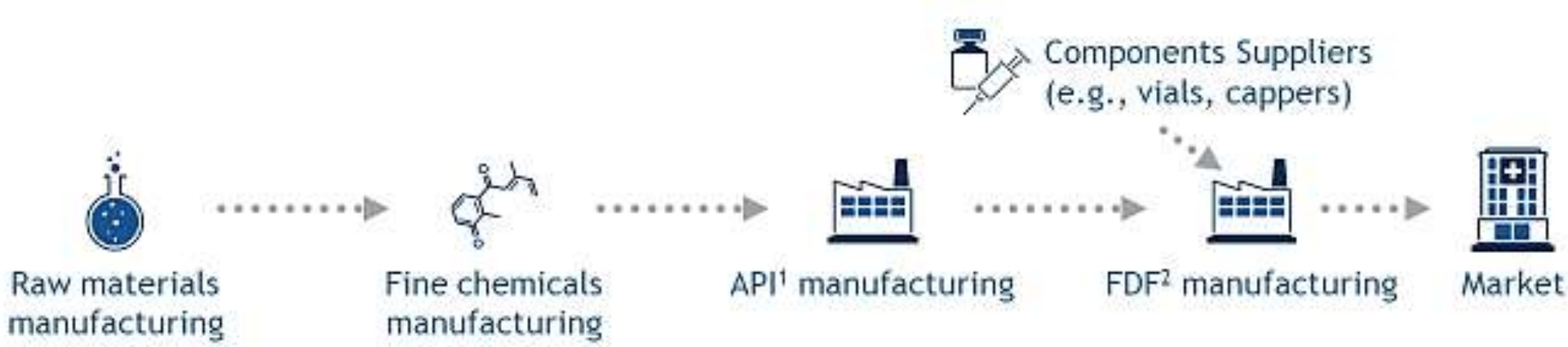
- Define Pharmaceutical Quality and its importance to patients
- Describe how FDA regulates pharmaceutical quality and the roles and responsibilities of Office of Pharmaceutical Quality

Pharmaceutical quality is

consistently meeting standards that ensure every dose is safe and effective, free of contamination and defects.

Pharmaceutical Quality is also linked to Drug Availability

- 2019 Drug Shortage Report
- Supply Chain Issues highlighted by the COVID-19 Crisis



A History of Events Affecting Quality

1938

>100 deaths from elixir sulfanilamide

1938 Food, Drug, and Cosmetic (FD&C) Act

Safety studies required for new drugs

1962

Children born with severe birth defects from thalidomide

1962 Kefauver-Harris Amendments to the FD&C Act

Need to prove that drugs are safe and effective

2015

>100 deaths from global heparin crisis in 2008
> 50% of shortages are due to quality issues

CDER establishes Office of Pharmaceutical Quality (OPQ) which integrates functions and elevates commitment to quality

2020+

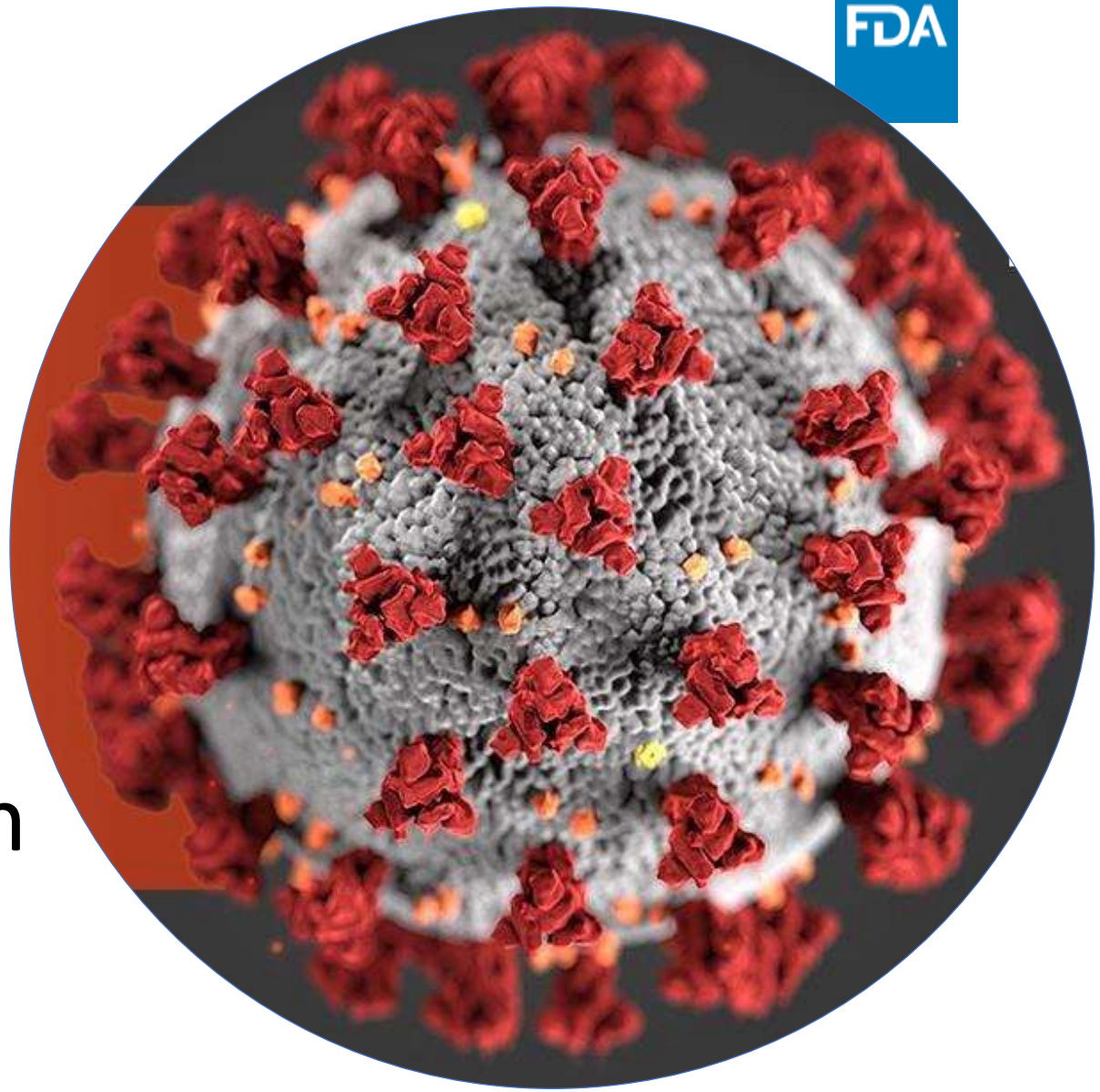
COVID-19 outbreak highlighted need for new drugs, repurposing existing drugs, supply pressures on essential medicines

Supply chain, Alternative tools for site evaluations, rapid approvals and authorizations for site changes, increased international collaborations

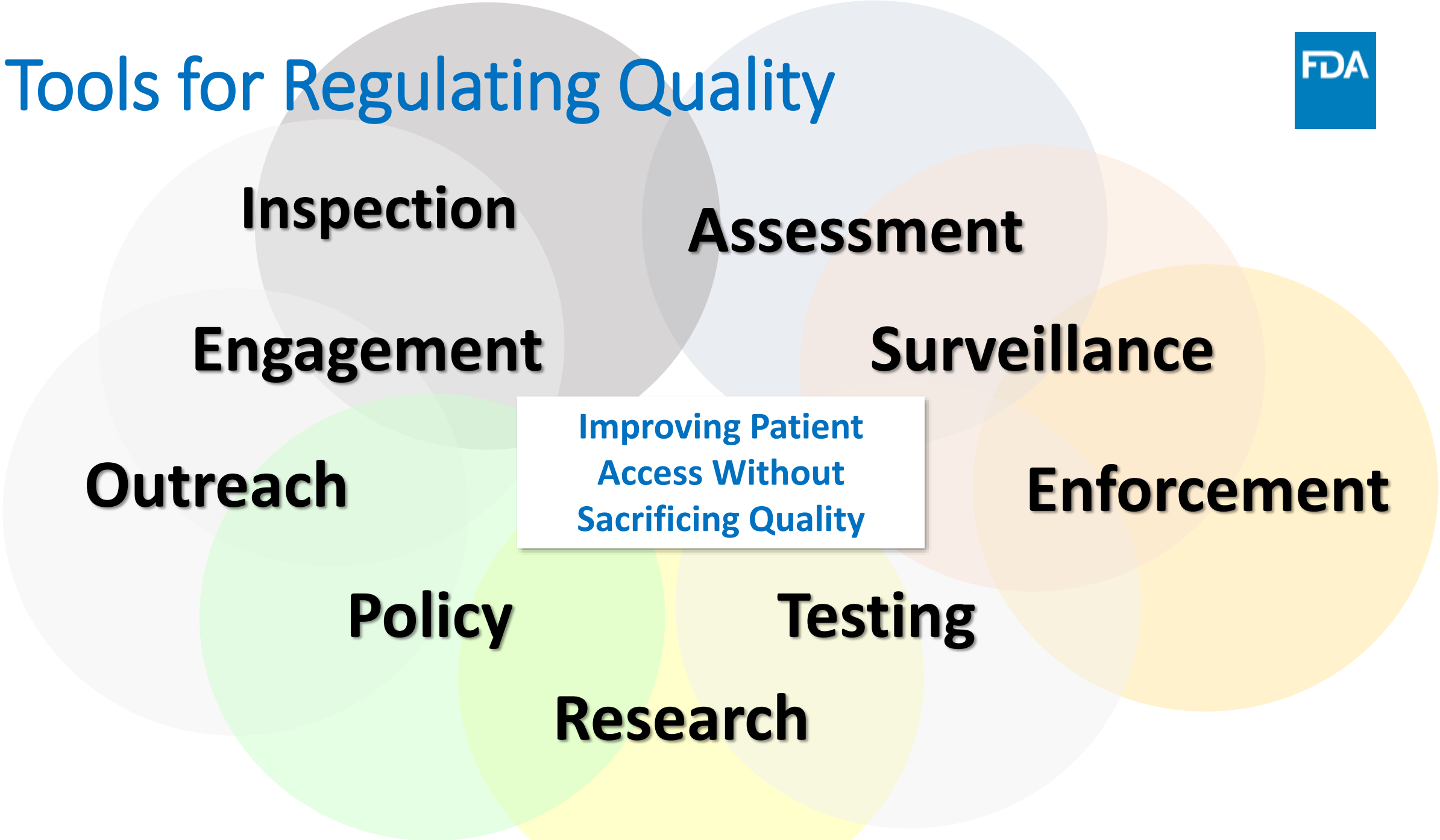
The Era of COVID-19

Long-existing quality issues are now magnified

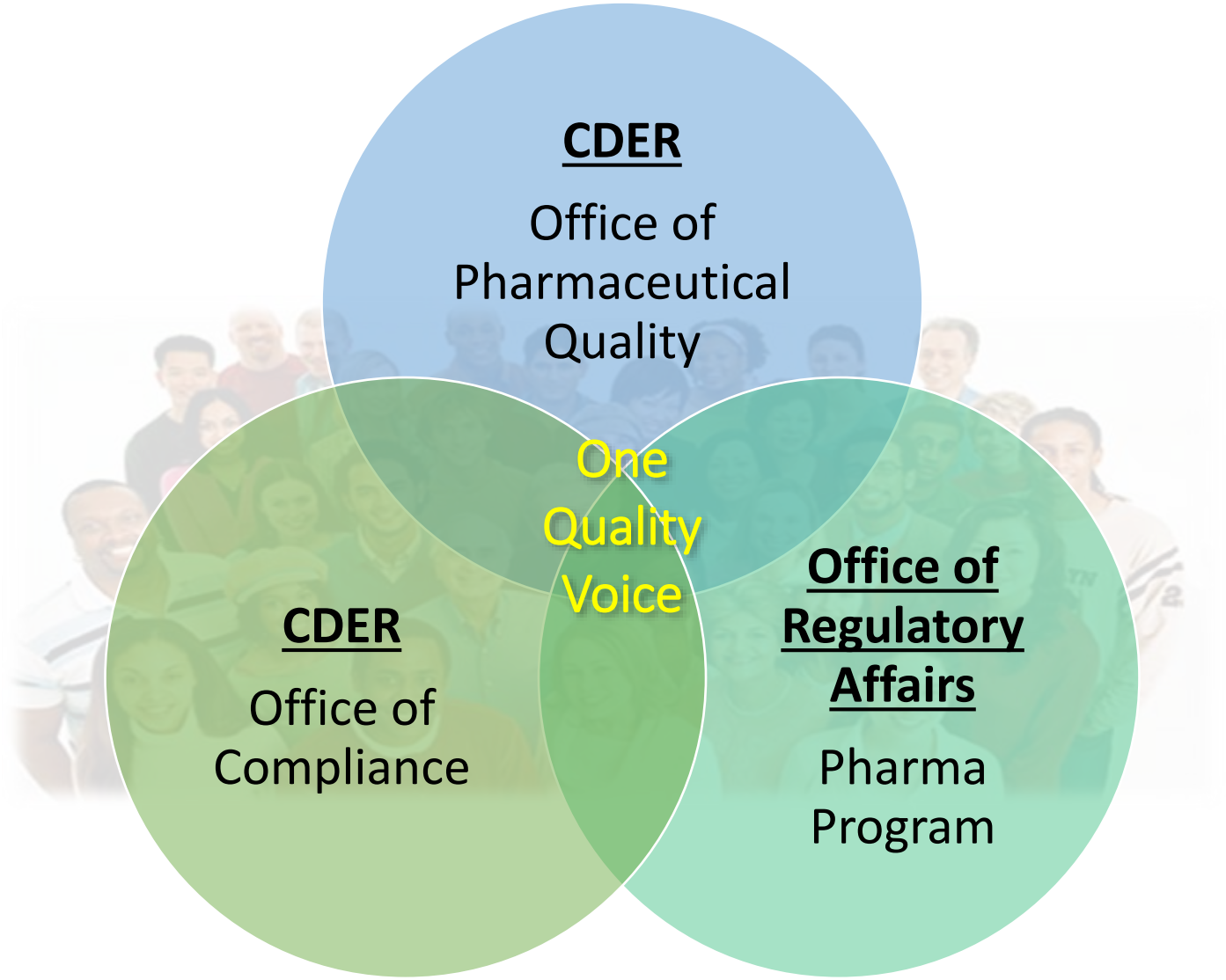
- Supply chains
- Shortages
- Decision-making based on changing science and risk



Tools for Regulating Quality



One Quality Voice



OPQ

Immediate Office
Michael Kopcha
Office Director

Adam Fisher
Acting Assoc. Director for Communications

Cindy Buhse
Deputy Super Office Director of Operations

Sau Larry Lee
Deputy Super Office Director of Science

Office of Administrative Operations (OAO)
Candee Chadwick

Office of Program and Regulatory Operations (OPRO)
Don Henry

Office of Policy for Pharmaceutical Quality (OPPQ)
Ashley Boam

Office of Biotechnology Products (OBP)
Steven Kozlowski

Office of New Drug Products (ONDP)
Lawrence Yu

Office of Quality Surveillance (OQS)
Jennifer Maguire

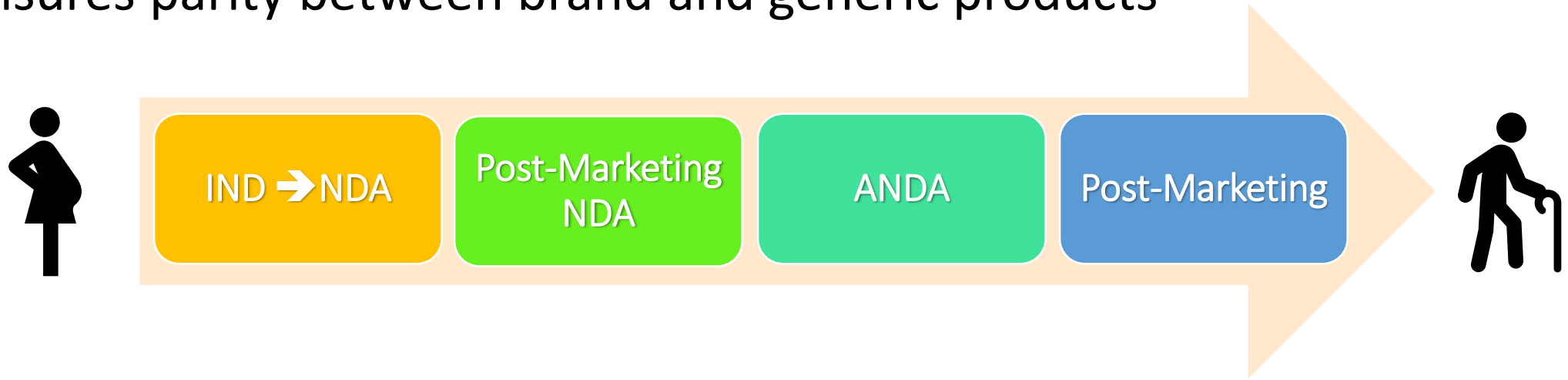
Office of Testing and Research (OTR)
David Keire

Office of Lifecycle Drug Products (OLDP)
Susan Rosencrance

Office of Pharmaceutical Manufacturing Assessment(OPMA)
Stellios Tsinontides

Quality Over the Drug Product Lifecycle

- **OPQ focuses on the entire drug product life**
- **We emphasize knowledge sharing across life stages**
  - Assures quality medicines are consistently available to the American public
  - Proactively works to prevent drug shortages
  - Ensures parity between brand and generic products



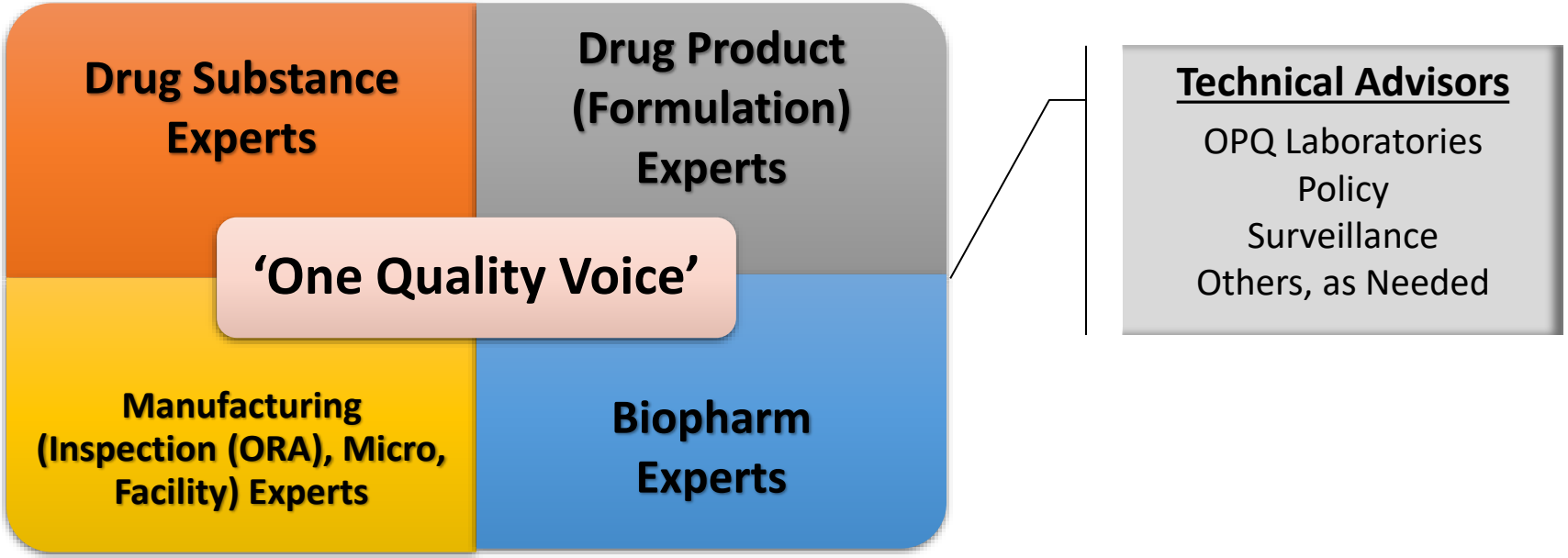
OPQ: By the Numbers

Around 1,300 staff in OPQ

- **Quality Assessments of submissions in a year:**
  - **Around 20 biologics including biosimilars**
  - **Around 200 new drugs**
  - **Around 3,000 investigational new drugs**
  - **Around 4,000 generics**
  - **Around 7,000 supplements**
- **Surveillance of ~6,000 facilities including non application products**
- **>100 Publications and >200 Technical Reports per year**
- **Numerous policy documents for internal and external use**

Team-based Integrated Quality Assessment (IQA)

Discipline Reviewers



Application Technical Lead (ATL) – oversees the scientific content of the assessment
Regulatory Business Process Manager (RBPM) – manages the process, keeps team on track to meet established timelines, and communicates with sponsors

Human Drug Inventory by Approximate Numbers

Sites:

- ~7,950 human drug manufacturing sites of obligation (as defined by regulations and policy)
  - ~1,840 Medical Gas (MG) manufacturers (nearly all in U.S.)
  - ~6,110 Non-MG manufacturers
    - 46% domestic
    - 54% foreign

Products:

- 32,439 unique Products
  - Defined as combination of active Ingredient, dosage form and route of administration
- 21,767 unique Active Pharmaceutical Ingredients
- 58 unique medical gas by proprietary name

Note: *Based on August 2021 Surveillance Catalogs and current eDRLS listings.*

Sources of Information for Quality Surveillance

Facility and Inspection Data

- Registration and Listing
- Inspection findings
- Profile Class Codes, Imports, Business operations, etc.

Quality Defect Reports

- Field Alert Reports (FARs)
- Biological Product Deviation Reports (BPDRs)
- MedWatch Reports
- Recalls (Type I, II, III)
- Consumer Complaints
- Informants

Drug Quality Sampling and Testing Results

Application data

- Original and Supplements
- Annual Reports

External data

- Foreign regulatory authority information
- Public information – social media, consumer reviews (e.g., drugs.com), blogs, news outlets, etc.

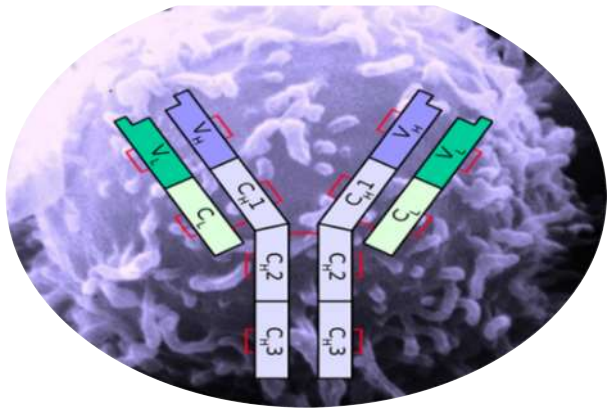
Future

Quality Metrics

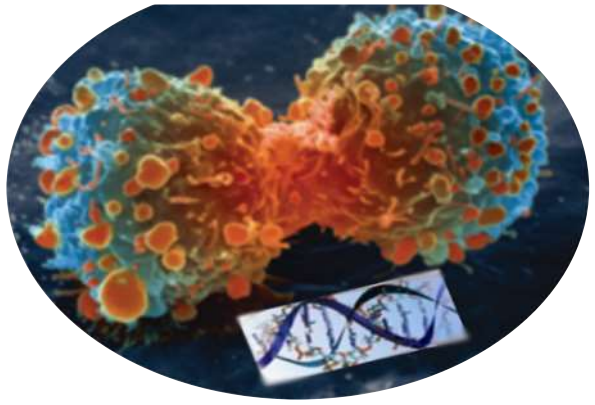
Quality Management Maturity

OPQ Science and Research

Immunology



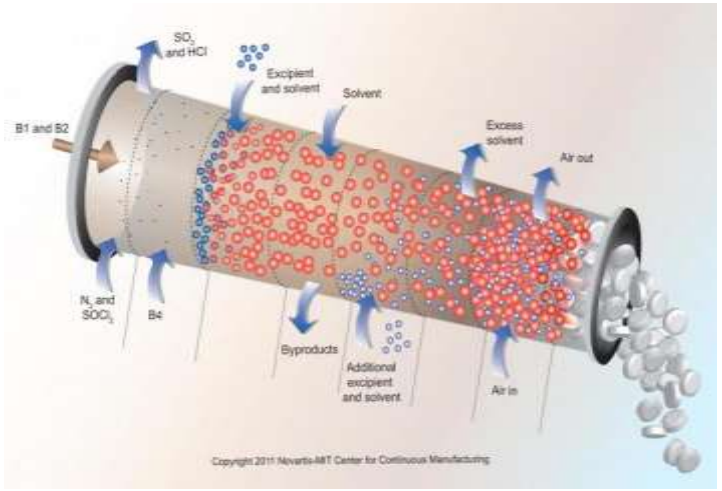
Tumor Biology



Manufacturing Science & Innovation

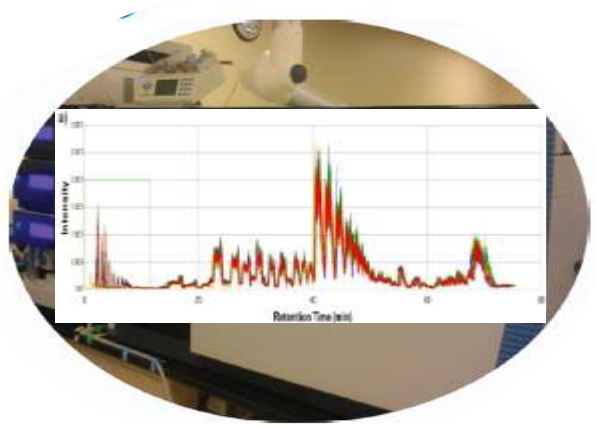
Novel **manufacturing methods** to improve process robustness and efficiency

Novel **dosage forms** or delivery systems to improve drug delivery and targeting

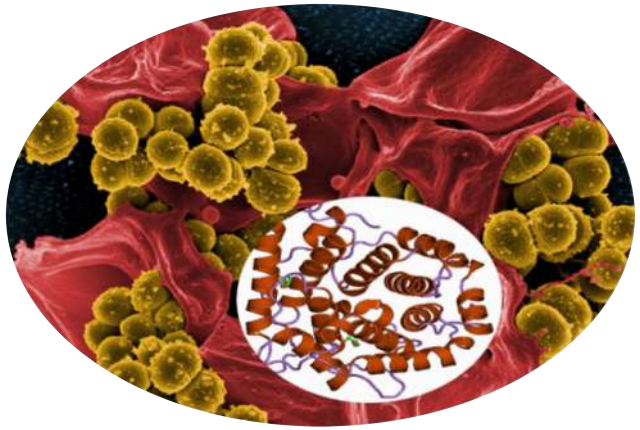


Pharmaceutical Analysis & Characterization

Novel **analytical tools** to improve product quality testing, process monitoring and/or control



Infectious Disease & Inflammation



The Future: Assuring Quality

- **Advanced Manufacturing Research and Regulatory Framework**
- **Pharmaceutical Supply Chain Understanding**
- **Quality Management Maturity Program**
- **Promote Regulatory Convergence**
- **Foster Global Partnerships**

Challenge Question #1

What percent of non medical gas pharmaceutical facilities are located in the US?

A. 10%

B. 20%

C. 46%

D. 80%

Challenge Question #2

Which of the following statements is true?

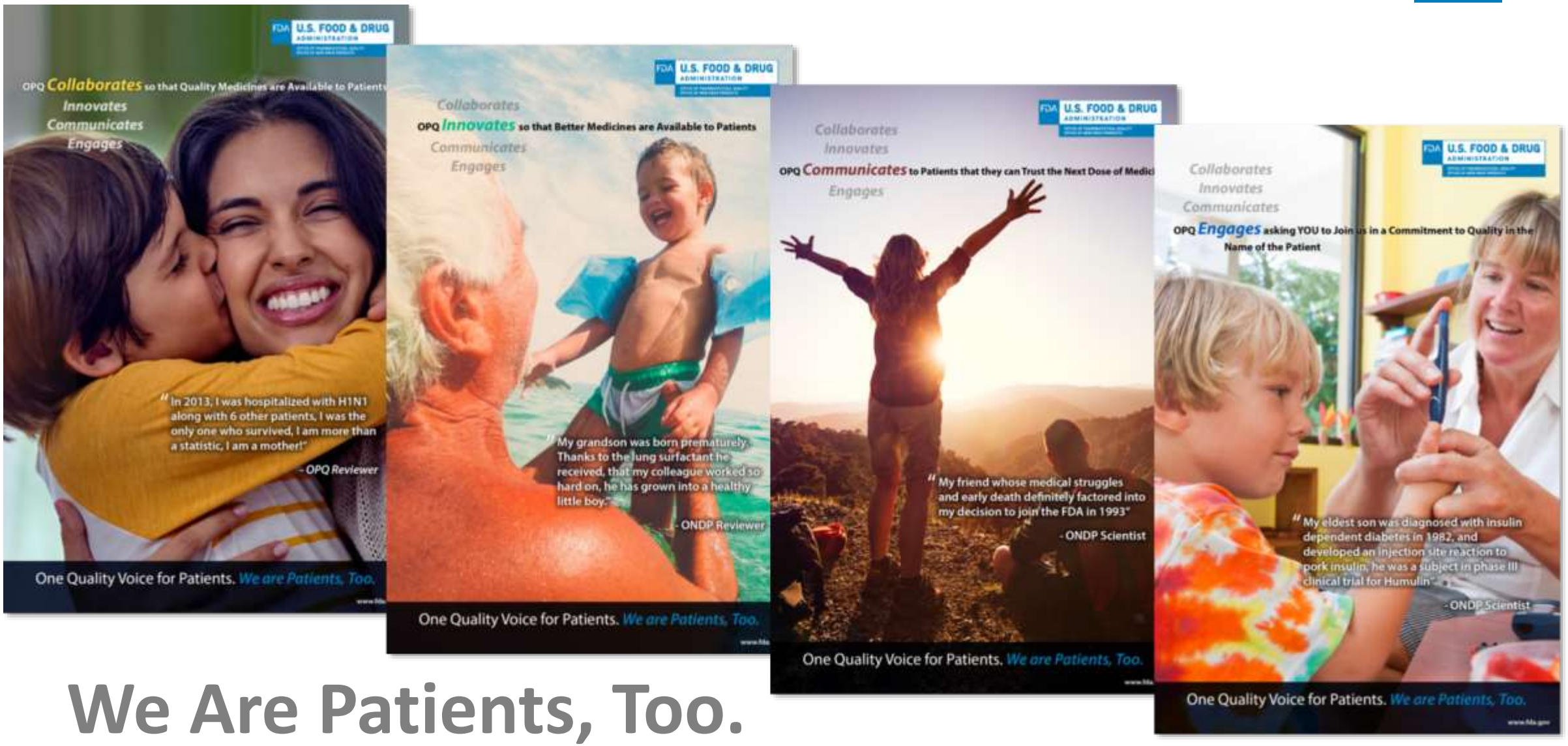
A. OPQ is responsible for clinical review of new drugs.

B. OPQ regulates pharmaceutical quality only for generic drugs.

C. OPQ regulates pharmaceutical quality only for small molecules (new drugs and generics).

D. OPQ regulates pharmaceutical qualify for small molecules (new drug and generics), biologics, and non application products (including some over-the counter and homeopathic products).

One Quality Voice for Patients



We Are Patients, Too.