Understanding How the Public Perceives and Values Pharmaceutical Quality

National Press Club

529 14th Street NW, Washington, DC 20045

February 3, 2020

Welcome & Overview

Opening Remarks from FDA

Introduction to Pharmaceutical Quality

U.S. FOOD & DRUG ADMINISTRATION

The Importance of Pharmaceutical Quality

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Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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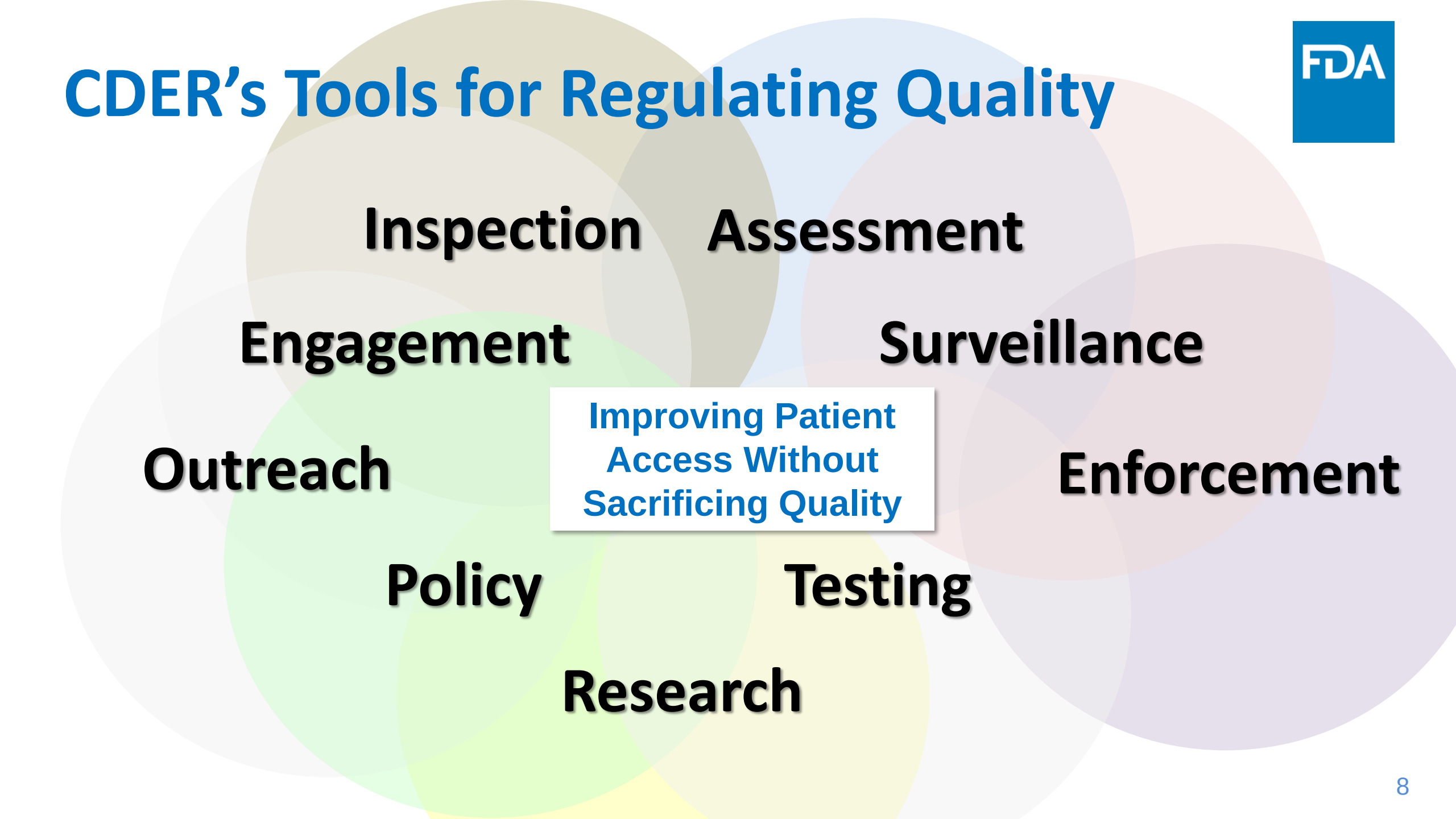
The Importance of Pharmaceutical Quality

- Pharmaceutical quality is what assures drugs on the market are safe and effective
- When quality goes wrong, everything can go wrong
- As we improve patient access to medicine, we cannot sacrifice quality

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.

CDER's Tools for Regulating Quality



Improving Patient Access Without Sacrificing Quality

- Expect consistent quality regardless of where a drug or its ingredients are manufactured
- Maintain the integrity of the supply chain in an increasingly complex and globalized environment
- Simplify regulatory processes and strive for international convergence on quality standards

Quality is a Partnership With Many Stakeholders

PAYERS

PATIENTS

PURCHASERS

CONSUMERS

PROVIDERS

YOU

TEACHERS

STUDENTS

MANUFACTURERS

COMPOUNDERS

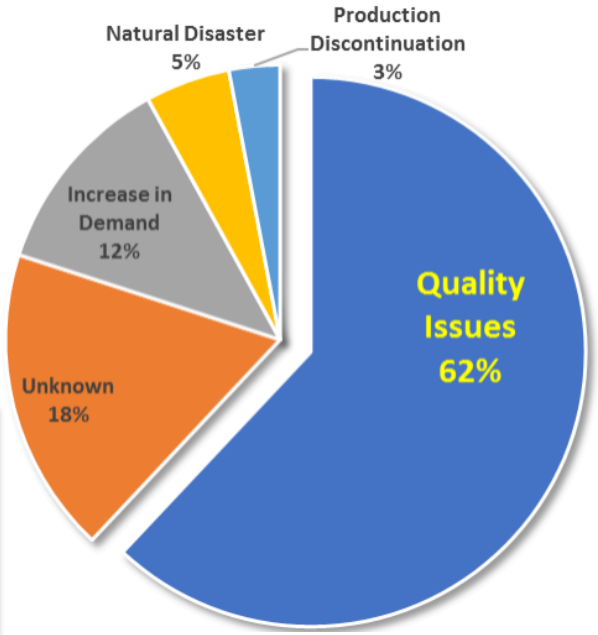
PHARMACISTS

INT'L REGULATORS

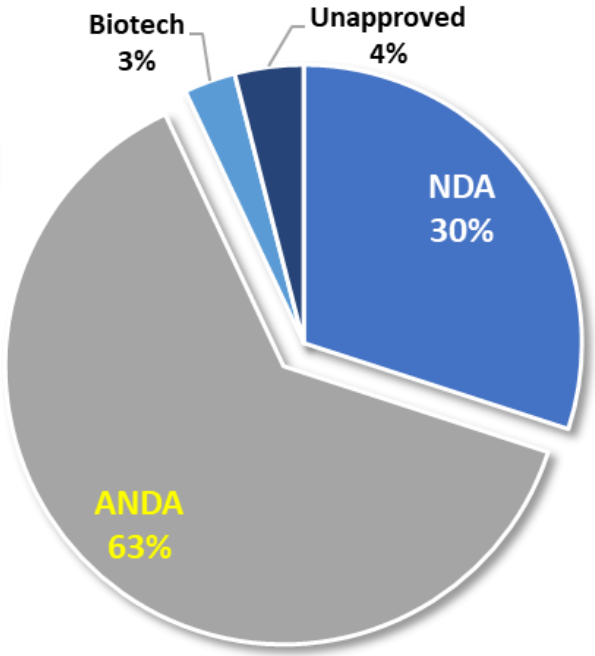
HOSPITALS

ENGINEERS

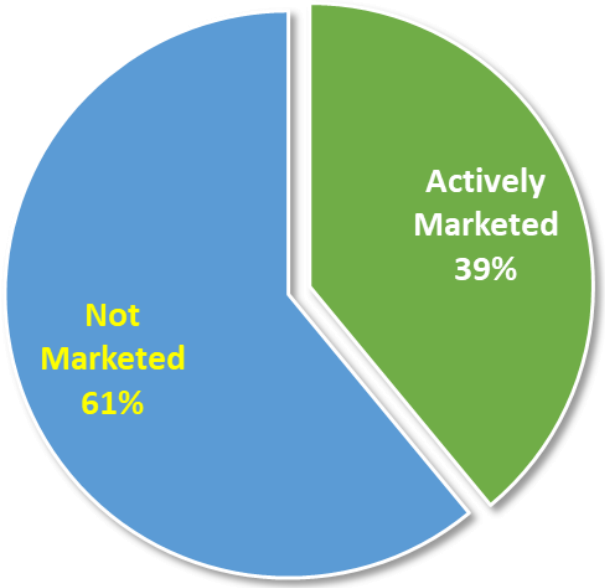
Drug Quality and Shortages



All Drugs Newly in Shortage



All Drug Products in Shortage



All Approved Generic Drug Applications

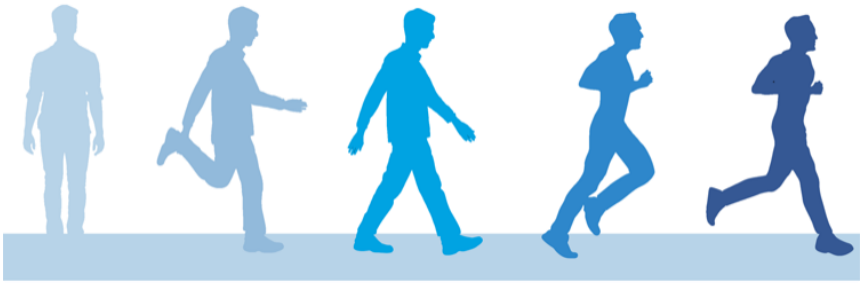
Incentivizing Investment in Quality Management Maturity

Root causes for drug shortages:

- Lack of incentives for manufacturers to produce less profitable drugs
- Market does not recognize and reward manufacturers for “mature quality systems”
- Logistical and regulatory challenges make it difficult to recover from a supply disruption

Quality Management Maturity

- **Basic Quality Management Systems**
  - *Reactive:* focused on Current Good Manufacturing Practice (CGMP) compliance
- **Strong, mature Quality Management Systems**
  - *Proactive:* focus on performance, especially outcomes that affect the patient



Transparency and Decision Making: Public Rating System

Enduring solutions:

- Understanding the impact of drug shortages and the contributing contracting practices
- A ‘rating system’ to incentivize quality management maturity
- Sustainable private sector contracts for a reliable supply of medically important drugs

Investing in Quality at the FDA

Investing in IT Solutions

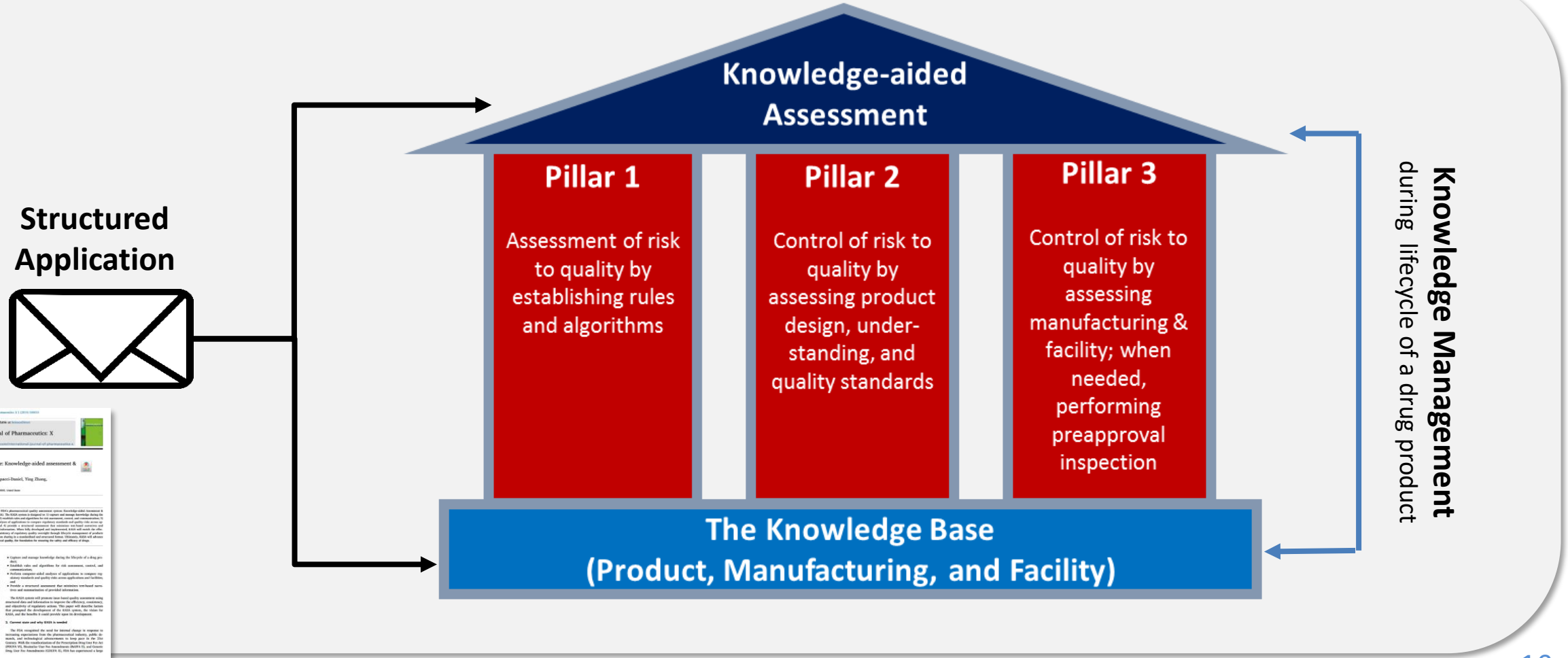
- Knowledge-aided Assessment and Structured Application (KASA)

Improving Inspections

- New Inspection Protocol Project (NIPP)

The KASA System

KASA – Knowledge-aided Assessment and Structured Application



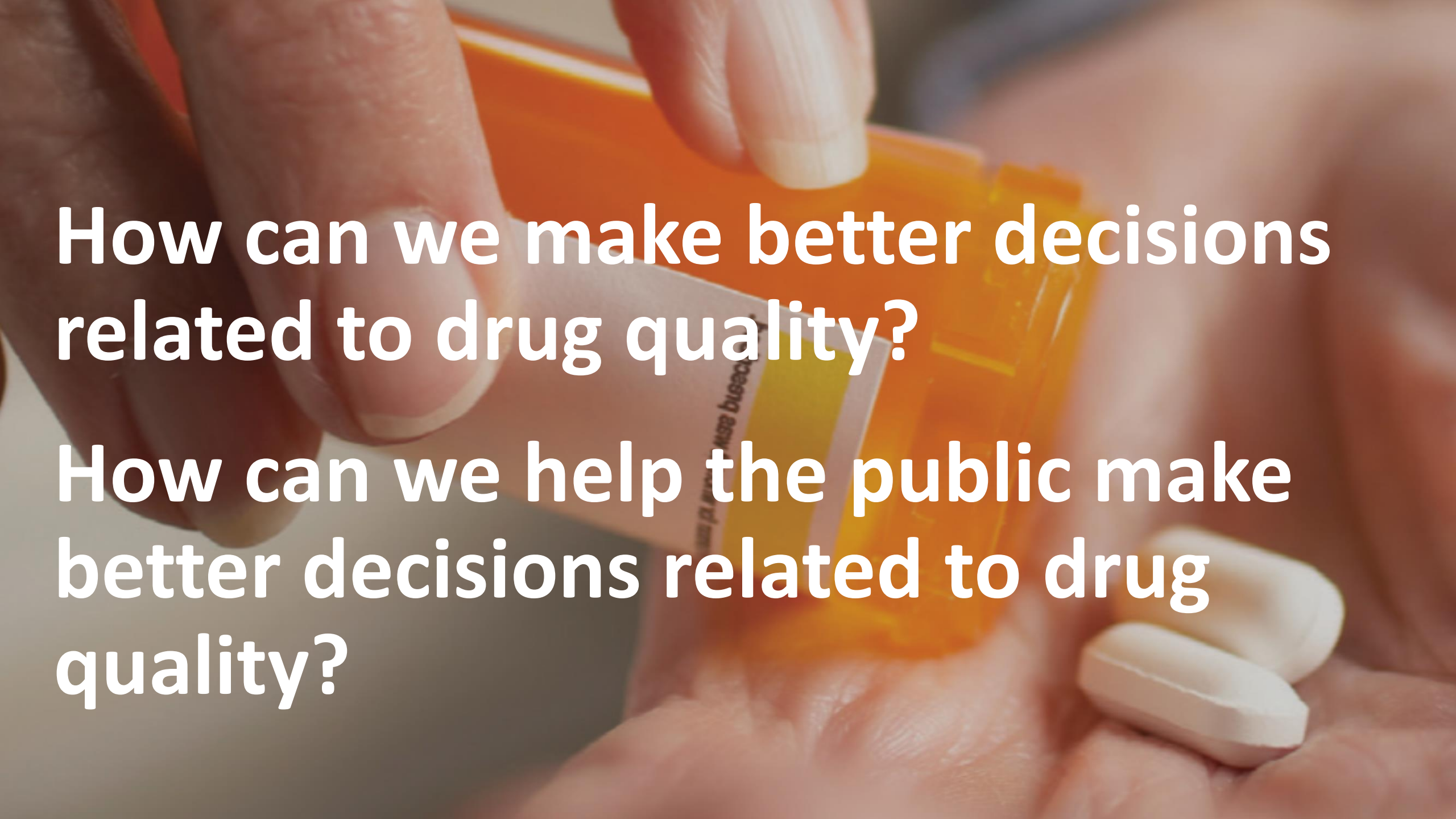

International Journal of Pharmaceutics: X

FDA's new pharmaceutical quality initiative: Knowledge-aided assessment & structured applications

*Read more: Yu, et al. *Int J Pharm* 2019

FDA's New Inspection Protocol Project (NIPP)

- **Paradigm to better assess and record the state of quality in manufacturing facilities**
  - Standardized electronic inspection protocols
  - Templated, semi-automated inspection reports
  - Quality maturity indicators



How can we make better decisions related to drug quality?

How can we help the public make better decisions related to drug quality?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ADMINISTRATION

Introduction to Pharmaceutical Quality

The Office Of Pharmaceutical Quality's Role in Regulating Quality

Michael Kopcha, Ph. D., R.Ph.
Director - Office of Pharmaceutical Quality
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Understanding How the Public Perceives and Values Pharmaceutical Quality
February 3, 2020

Office of Pharmaceutical Quality

new drugs

biologics

generics

compounded drugs

over-the-counter drugs

biosimilars

Development → Premarket → Postmarket

How Does OPQ Regulate Quality?

Before Application Approval

- Assess how the applicant develops, manufactures, and tests the active ingredients and final drug products
- When needed, address whether the product is sterile (microbiology)
- When needed, address whether the drug has the appropriate rate and extent of absorption after administration to the human body (biopharmaceutics)
- Assess whether the proposed facilities are appropriate and prepared for commercial manufacturing
  - When needed, may include an onsite, product-specific facility inspection

How Does OPQ Regulate Quality?

Beyond Application Approval

- Develop standards and policies based on science and benefit/risk
  - Also for over-the-counter drugs and certain compounded drug products
- Conduct research to support the development of science-based quality policies and standards
- Oversee quality throughout the lifecycle of a drug product by assessing changes proposed after application approval
- Monitor the state of quality for all regulated manufacturing sites and drug products
  - Develop a risk-ranking of all manufacturing sites to guide inspection planning

Assessing New Drugs vs. Generics

Brand-Name Drug Approval Requirements	Generic Drug Approval Requirements
Drug Substance	Drug Substance
Drug Product	Drug Product
Manufacturing Process	Manufacturing Process
Manufacturing Facilities	Manufacturing Facilities
Microbiology	Microbiology
Biopharmaceutics	Biopharmaceutics
Labeling	Labeling
Animal Studies	Bioequivalence
Clinical Studies	

Quality elements are the same

Clinical elements are different

The Pharmaceutical Quality Lifecycle

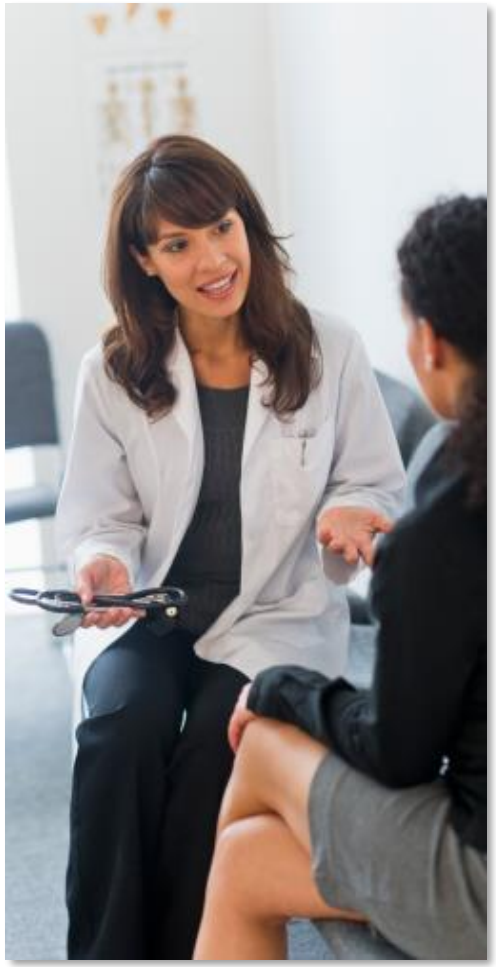
With a staff of ~1,300 OPQ's quality assessments average in a given year:

- **Around 20 biologics**
- **Around 200 new drugs**
- **Around 3,000 investigational new drugs**
- **Around 4,000 generics**
- **Around 7,000 supplements**

The State of Pharmaceutical Quality

- **OPQ continuously monitors the quality of all CDER-regulated drugs**
- **We now publish a yearly ‘snapshot’ of the industry’s ability to deliver quality pharmaceuticals**
- **This snapshot provides an objective assessment, using the quality indicators we can share with the public**
    - Based on available FDA drug product-specific and manufacturing site-specific data

Stakeholder Input



- **OPQ makes decisions in the name of <u>patients and consumers</u> not drug companies**
- **We need better understanding of physician and consumer knowledge and perception of drug quality**
- **We teamed up with WebMD to begin learning from U.S. consumers and physicians**

The Shortage Issue

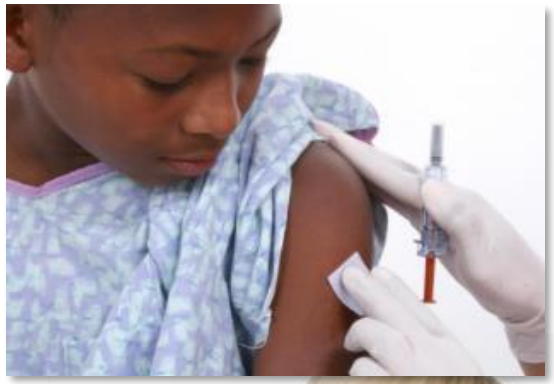
Root causes for drug shortages:

- Lack of incentives for manufacturers to produce less profitable drugs
- Market does not recognize and reward manufacturers for "mature quality systems"
- Logistical and regulatory challenges make it difficult to recover from a **supply disruption**

Enduring solutions:

- Understanding the impact of drug shortages and the contributing contracting practices
- A 'rating system' to incentivize quality management maturity
- Sustainable private sector contracts for a **reliable supply** of medically important drugs

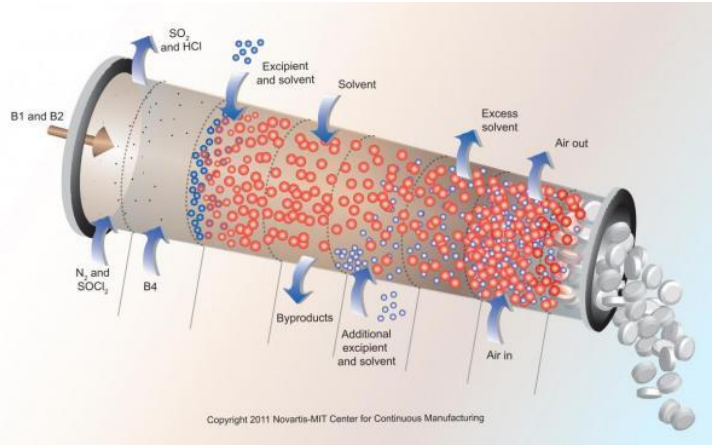
Modernizing Pharmaceutical Manufacturing

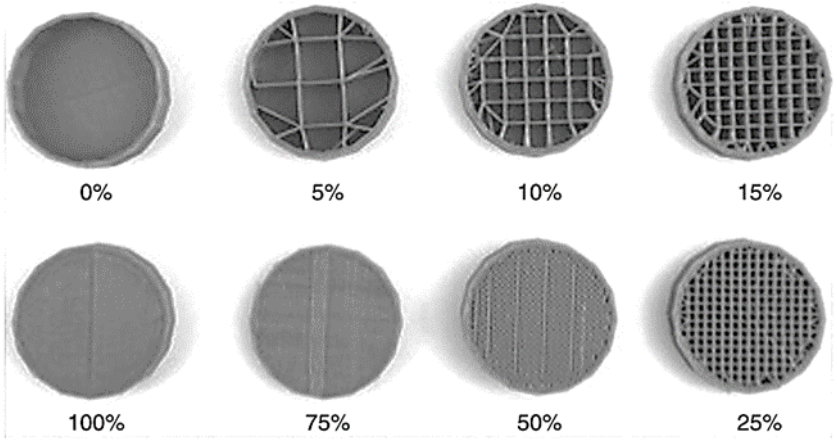


- **Consumers and patients deserve quality products with minimal risks of shortages or recalls**
- **Quality of manufacturing in pharma lags other industries (e.g., semiconductors >six sigma)**
- **CDER's Emerging Technology Program encourages and supports the adoption of innovative technology in pharmaceutical development and manufacturing**

What is Advanced Manufacturing?

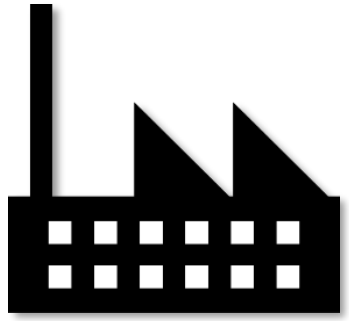
- Innovative **manufacturing technology** or approach that can enhance drug quality, improve the reliability and robustness of the manufacturing process and supply chain, and increase timely access to quality medicines for the American public
- Novel **dosage forms** or delivery systems to improve drug delivery and targeting
- Novel **analytical tools** to improve product quality testing, process monitoring and/or control



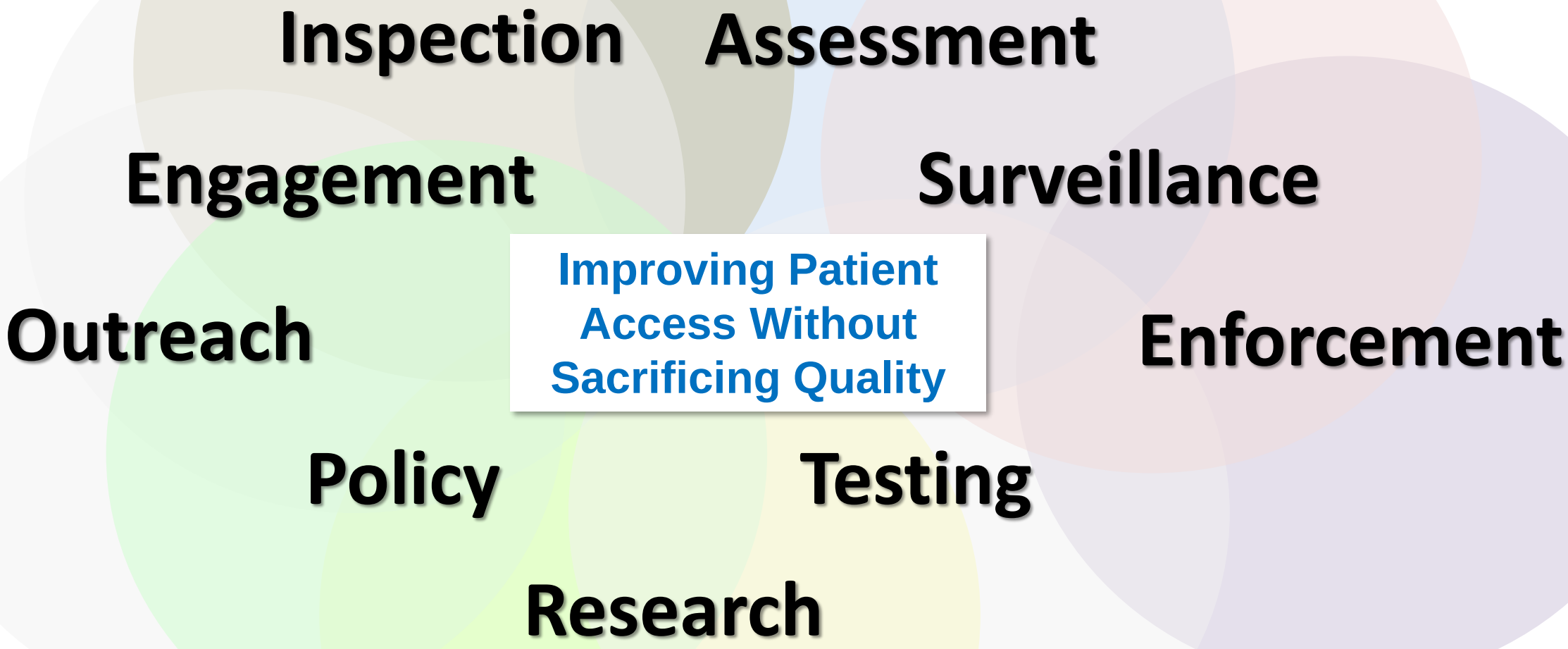


Why is Advanced Manufacturing important for both FDA and pharmaceutical industry?

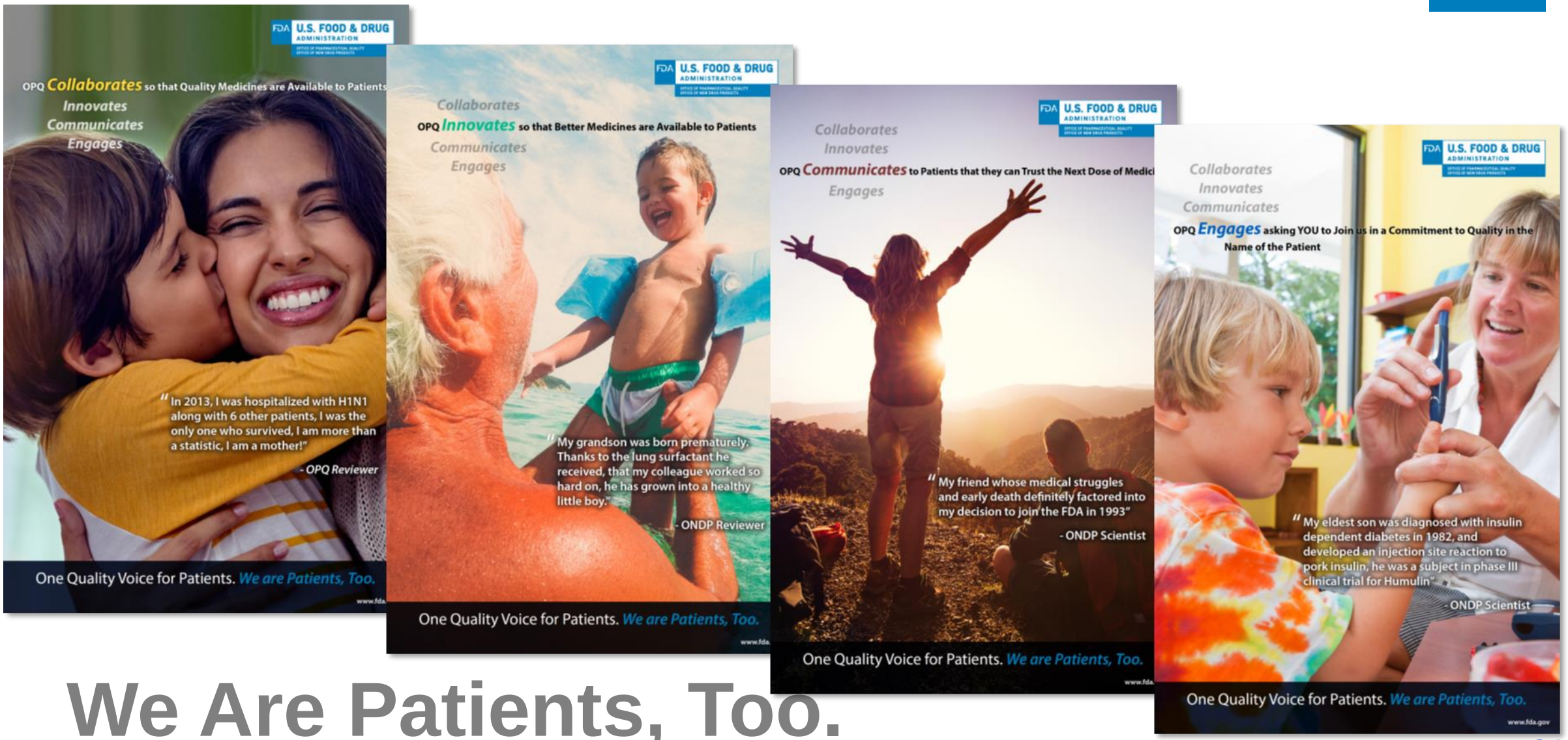
- **Addresses the <u>underlying causes of drug shortages</u>**
  - Helps mitigate or prevent future production problems
- **Facilitates <u>new clinical modalities</u>**
  - Precision and individualized medicines
  - A wider range of novel dosage forms and doses - without extensive alterations of the process
  - Convenient fixed-combination dosage forms
- **Improves <u>manufacturing efficiency</u>**
  - Increase process robustness
  - Lower manufacturing costs
  - Increase supply chain flexibility



CDER's Tools for Regulating Quality



One Quality Voice for Patients



We Are Patients, Too.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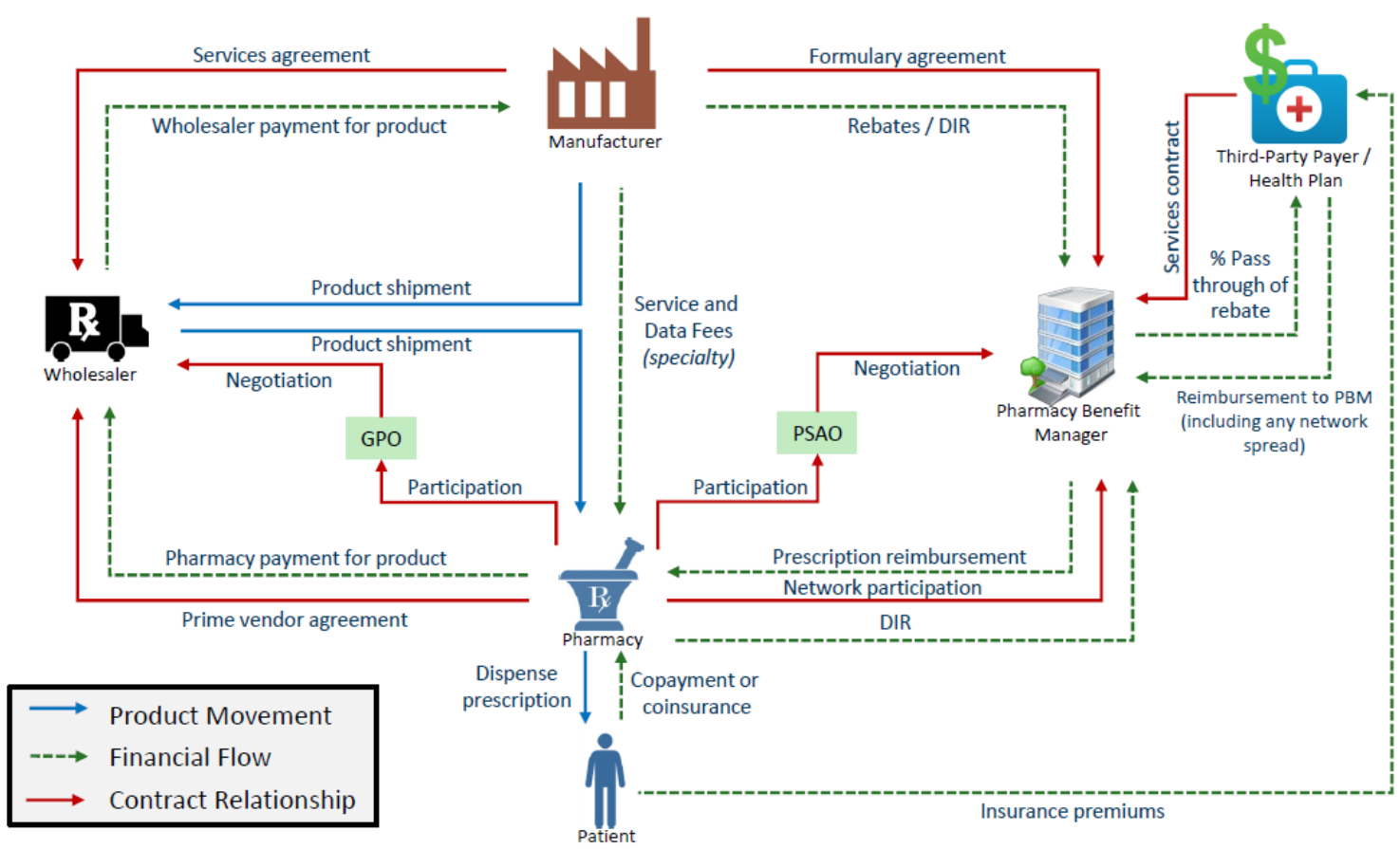
Introduction to Pharmaceutical Quality

The State of Pharmaceutical Quality

Report on the State of Pharmaceutical Quality

Cindy Buhse
Director, Office of Quality Surveillance
FDA/CDER/Office of Pharmaceutical Quality
Understanding How the Public Perceives and Values Pharmaceutical Quality
February 3, 2020

U.S. Drug Distribution & Reimbursement System Is Complex, Private Contracts Are Opaque



GPO = Group Purchasing Organization; PSAO = Pharmacy Services Administrative Organization; DIR = Direct and indirect remuneration
Source. *The 2019 Economic Report on U.S. Pharmacies and Pharmacy Benefit Managers* (https://drugch.nl/pharmacy). Chart illustrates flows for Patient-Administered, Outpatient Drugs. Please note that this chart is illustrative. It is not intended to be a complete representation of every type of product movement, financial flow, or contractual relationship in the marketplace.

Wall Street Journal

CDER/OPQ'S Office of Quality Surveillance

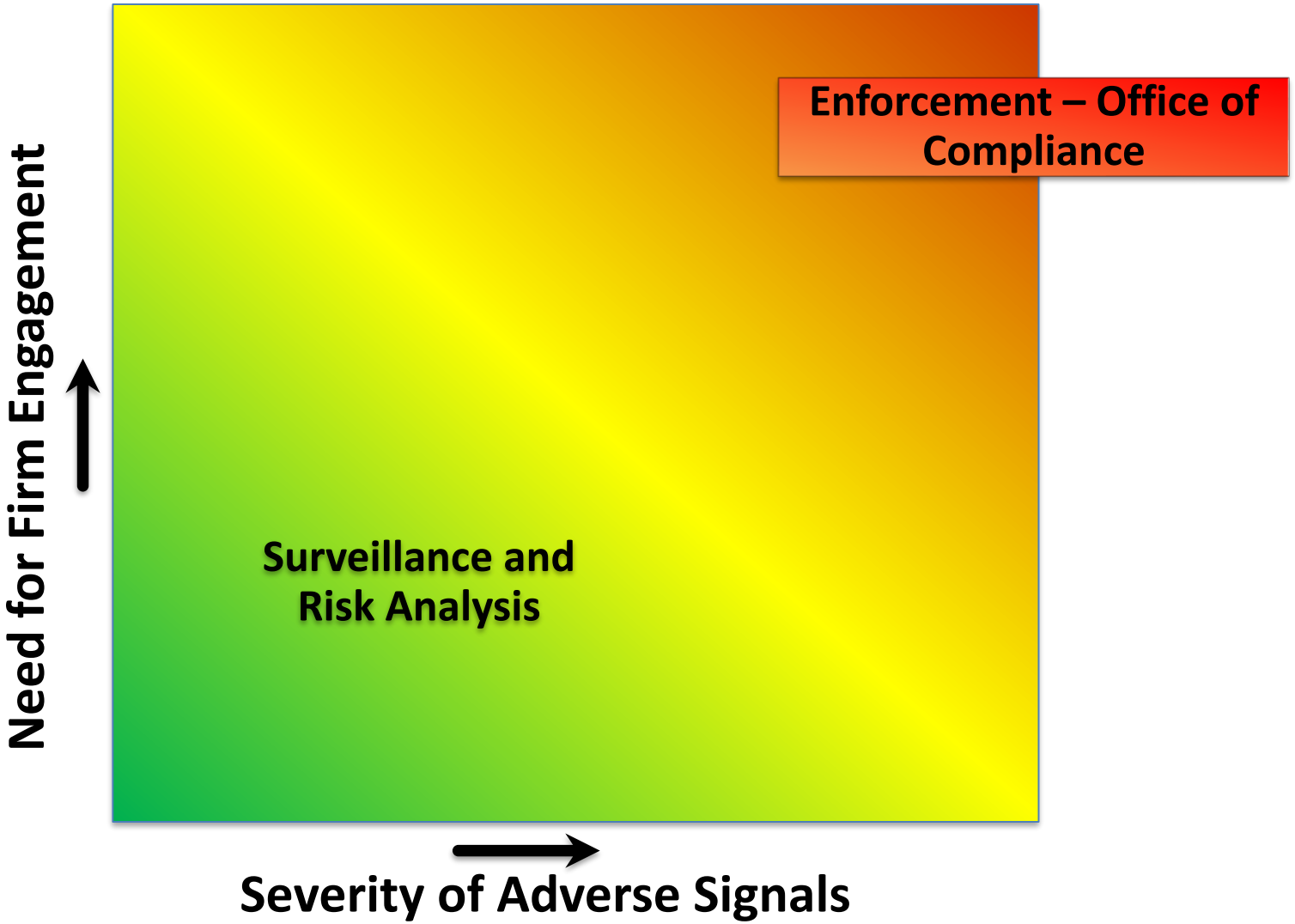
Sources of Information for Quality Surveillance

- **Facility and Inspection Data**
- **Quality Defect Reports**
  - MedWatch Reports
  - Recalls
  - Consumer Complaints
  - Industry quality report submissions
- **Drug Quality Sampling and Testing Results**
- **Application data**
- **External data**
  - Foreign regulatory authority information
  - Public information – social media, consumer reviews (e.g., drugs.com), blogs, news outlets, etc.

General Overview of Surveillance Activities

- Characterize the population of CDER-regulated sites and the products they manufacture
- Monitor and assess the state of quality
- Proactively identify potential quality signals and trends before serious quality problems occur

Surveillance vs Enforcement



Human Drug Inventory by Approximate Numbers

Facilities:

- ~6,000 human drug manufacturing sites
  - ~2,000 Medical Gas (MG) manufacturers (nearly all in U.S.)
  - ~4,000 Non-Medical Gas manufacturers
    - 44% domestic
    - 56% foreign

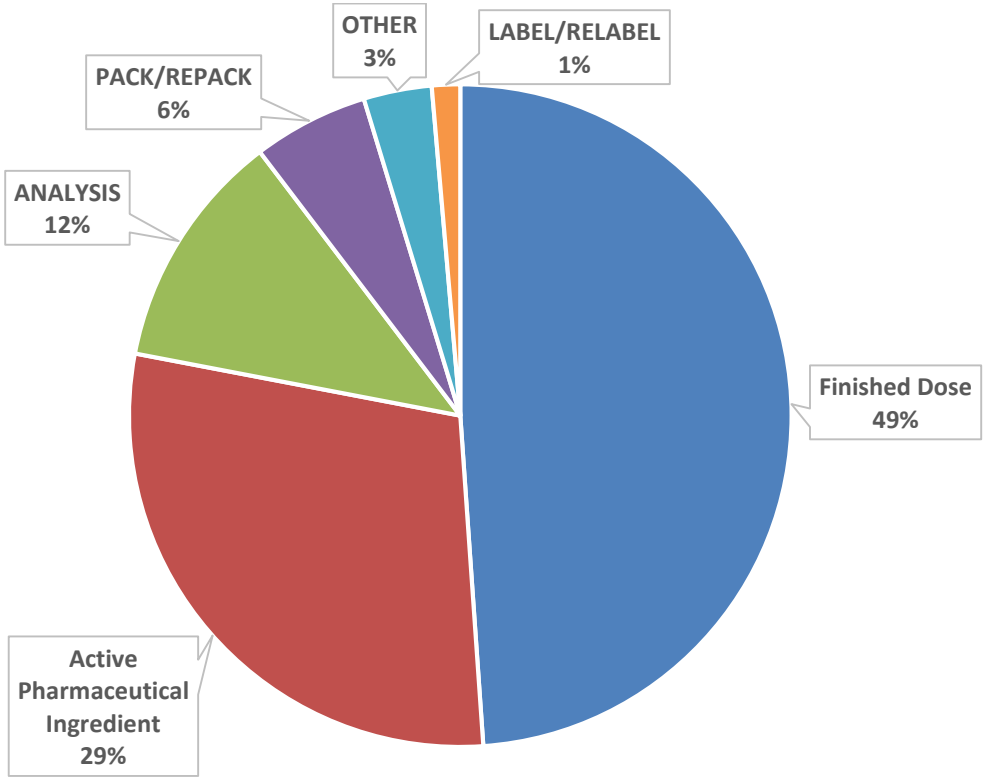
Products:

- 120,000 unique finished dose
- 35,000 unique Active Pharmaceutical Ingredients

Note: *Based on July 2019 Surveillance Catalogs and current eDRLS listings.*

Drug Manufacturing Facilities

- Excluding medical gas, 4060 sites are in the catalog as of July 2019. Facilities enter and leave the market daily (registrations, deregistrations, application approvals).
  - Domestic: 1782 sites
  - Foreign: 2278 sites
    - China: 347 sites
    - India: 476 sites
    - Rest of the World: 1455 sites

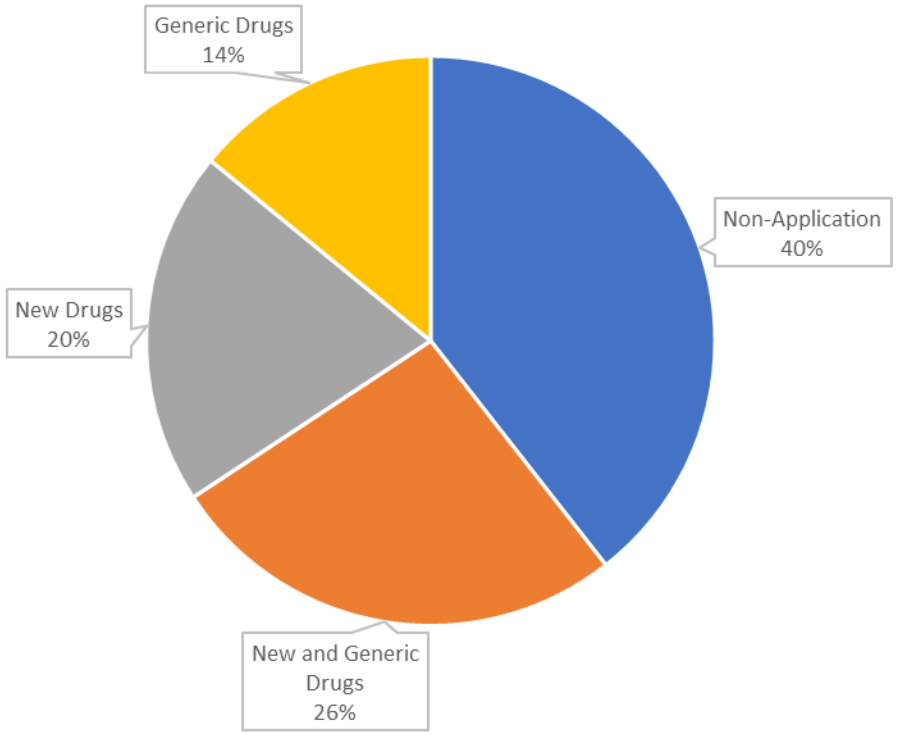


* The hierarchy for this analysis tags a site that makes both FDF and API as FDF facilities and a facility that makes both application and non application products as an application site.

Facilities by Drug Product Types

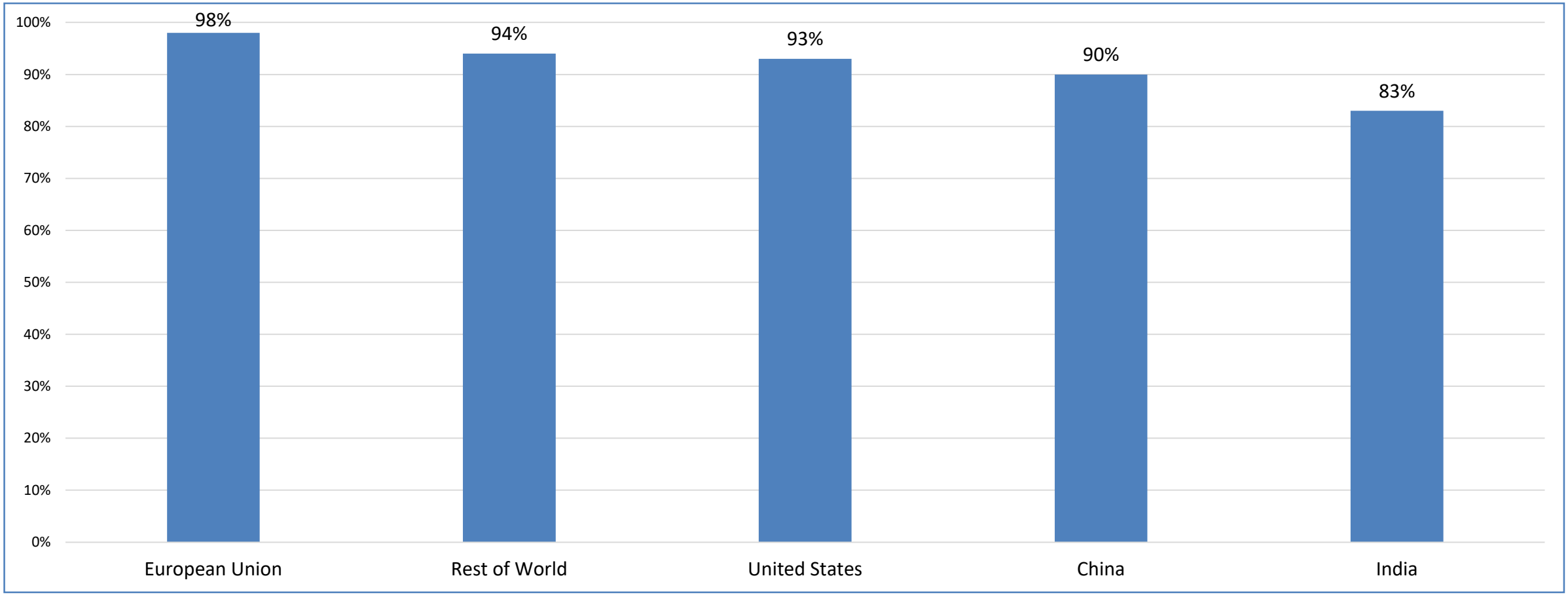
- Facilities* are also categorized through a hierarchy of industry sectors:
  - 20% of all facilities are listed in new and biotech drug applications only
  - 14% of all facilities are listed in generic drug applications only
  - 26% of all facilities are listed in both generic and new drug applications
  - The remaining 60% of facilities are not listed in any applications (non-application sites including some over-the-counter and homeopathic products)

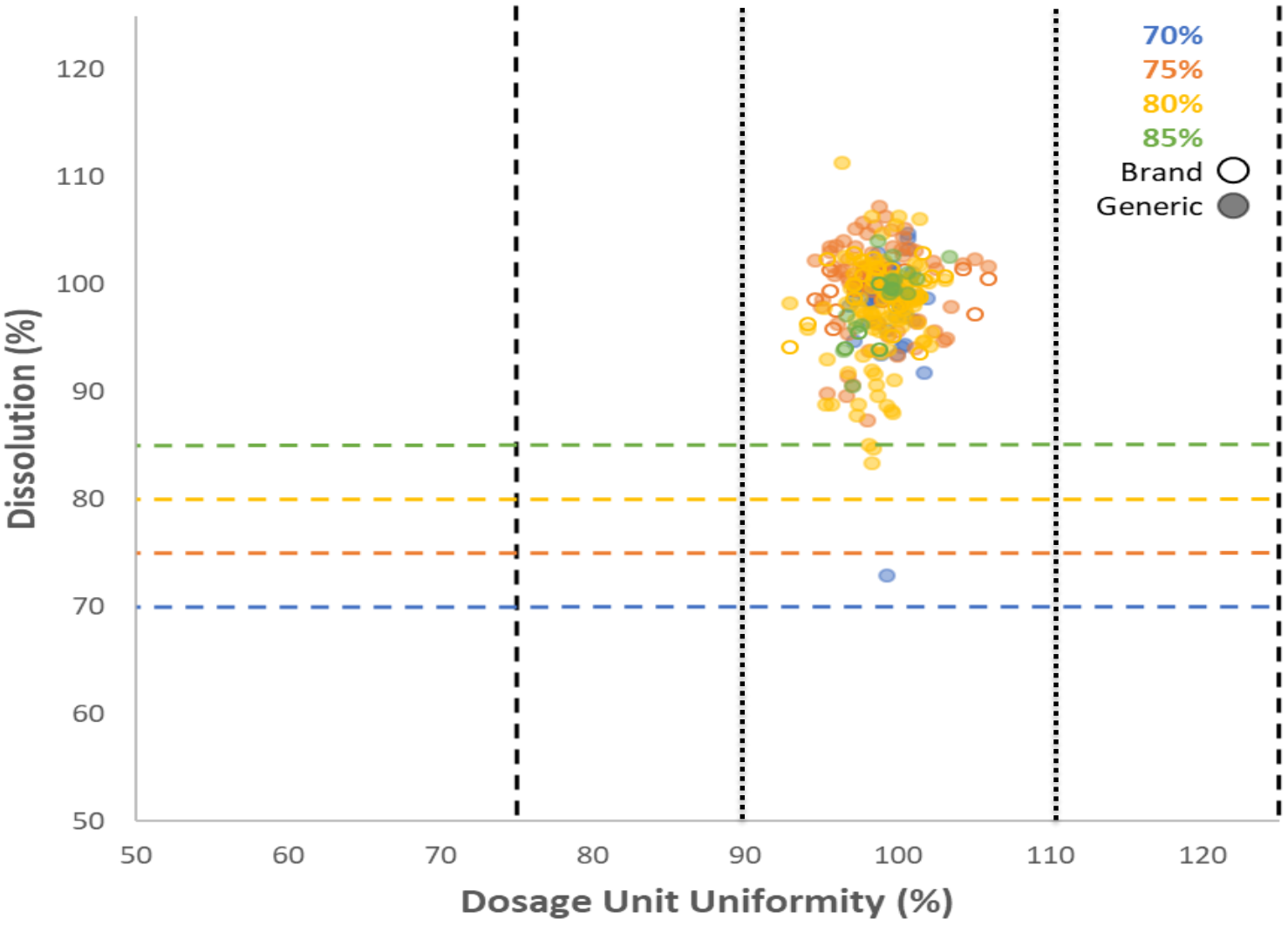
- **60% of all facilities are listed in application products**
- **40% of all facilities manufacture non-application products**



* Medical Gas not included

% of Manufacturing Facilities with Acceptable Final Outcome, as of August 2019





Surveillance Testing

252 Immediate Release Samples:
17 Active Ingredients
> 40 firms
5 regions
brand and generic

Colors represent different USP market standard criteria for dissolution.
Lines represent USP market standard criteria for dissolution and dosage unit uniformity

Public Information with FDA Access Links

- Inspections Classification Database

https://www.accessdata.fda.gov/scripts/inspsearch/

- Drug Shortages

https://www.accessdata.fda.gov/scripts/drugshortages/Drugshortages.cfm

- Drug Recalls

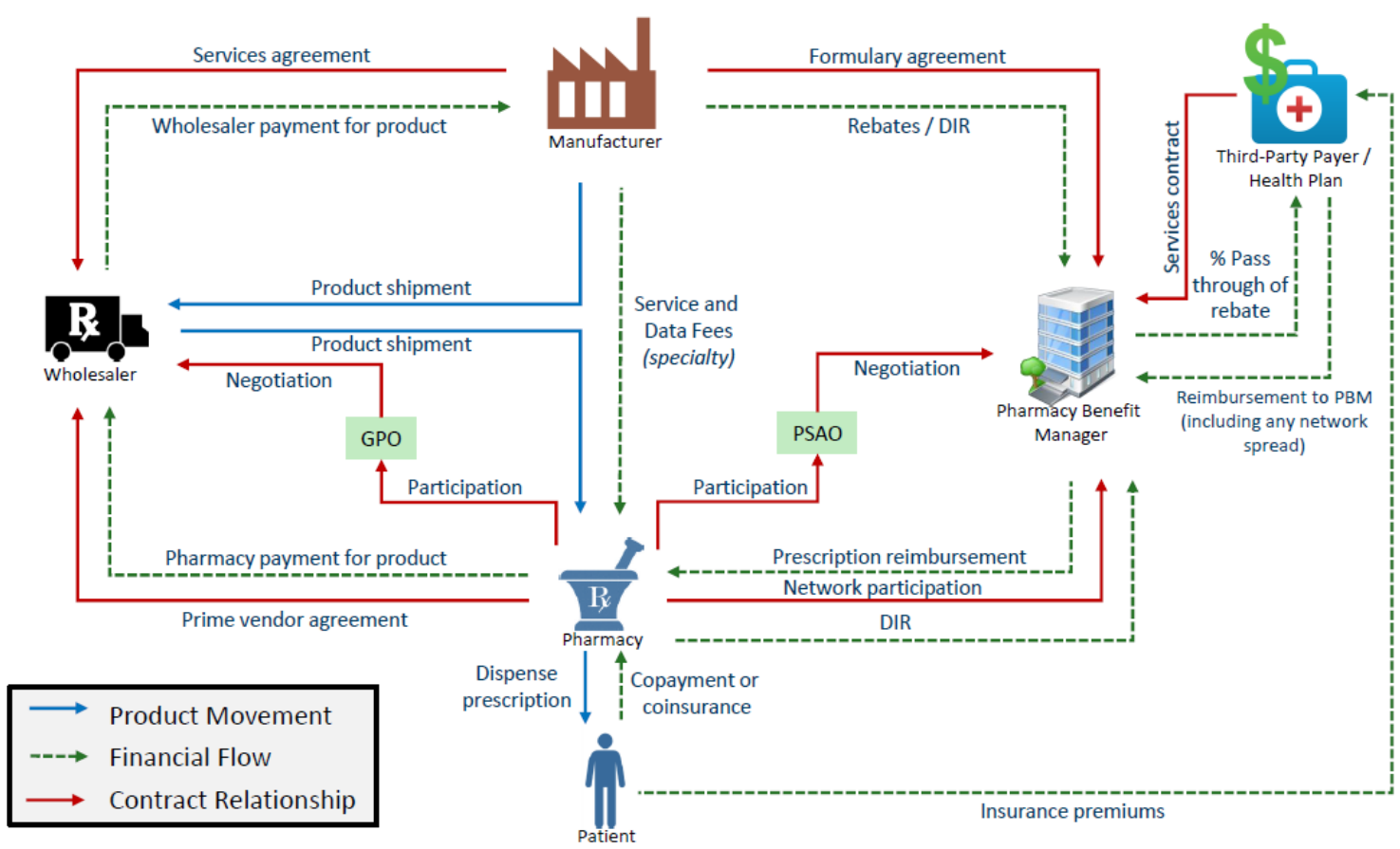
https://www.fda.gov/drugs/drug-safety-and-availability/drug-recalls

- Drug Quality Sampling and Testing Programs

https://www.fda.gov/drugs/science-and-research-drugs/drug-quality-sampling-and-testing-programs

- FDA Social Media

U.S. Drug Distribution & Reimbursement System Is Complex, Private Contracts Are Opaque



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Wall Street Journal

Take Aways

- OQS continually explores innovative ways to inform risk-based decisions.
- Some quality information is publicly available; however, there is a lack of transparency between facilities and products.
- OQS continues to engage stakeholders and support related academic research. Our goal is to keep all sites in compliance and all products available for the patient.
- **OQS monitors the state of quality for sites and products so every dose is safe and effective, free of contamination and defects and patients can be confident in their next dose.**


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The State of Pharmaceutical Quality

Patient and Provider Perceptions of Pharmaceutical Quality

Adam Fisher, Ph.D.
Office of Pharmaceutical Quality
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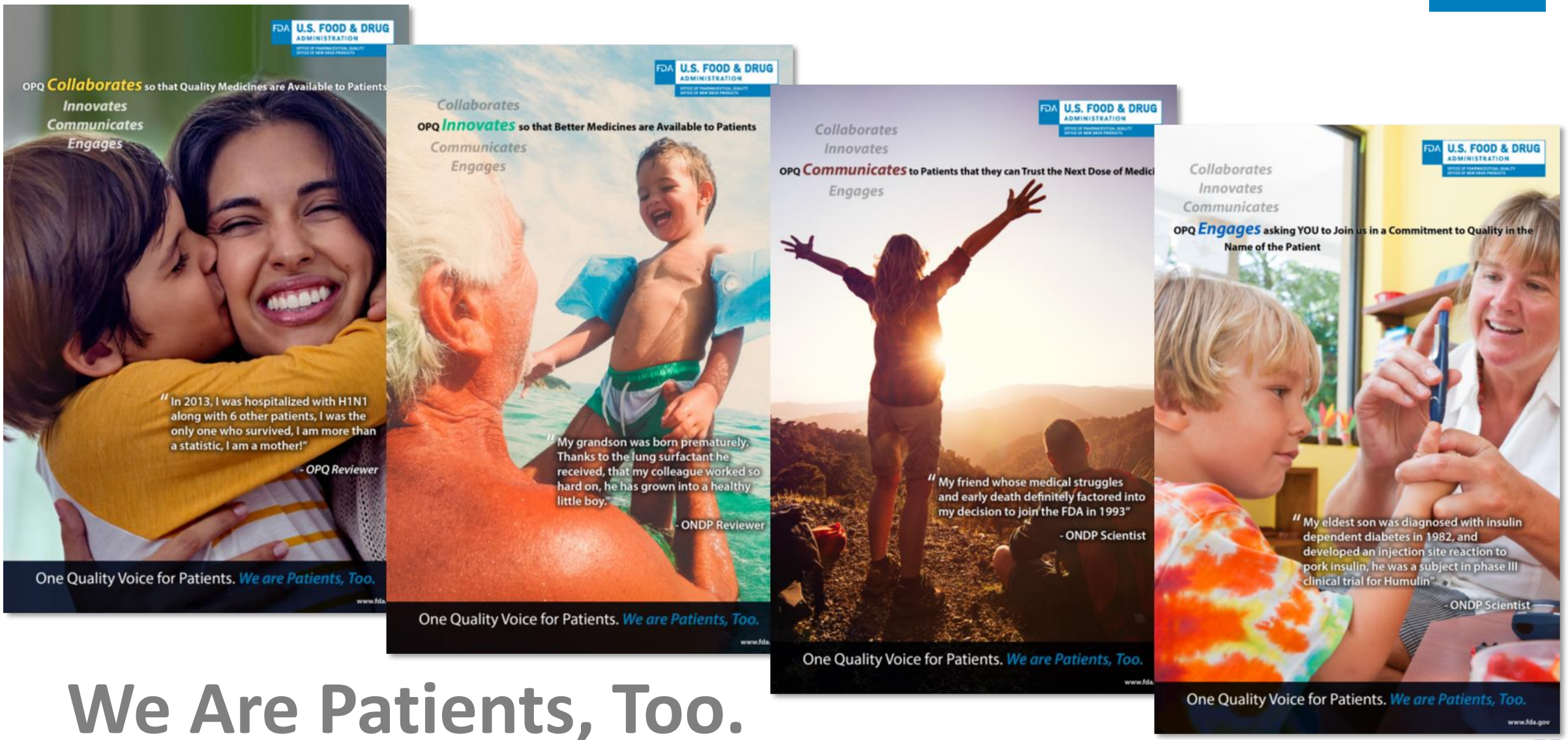
U.S. Food and Drug Administration

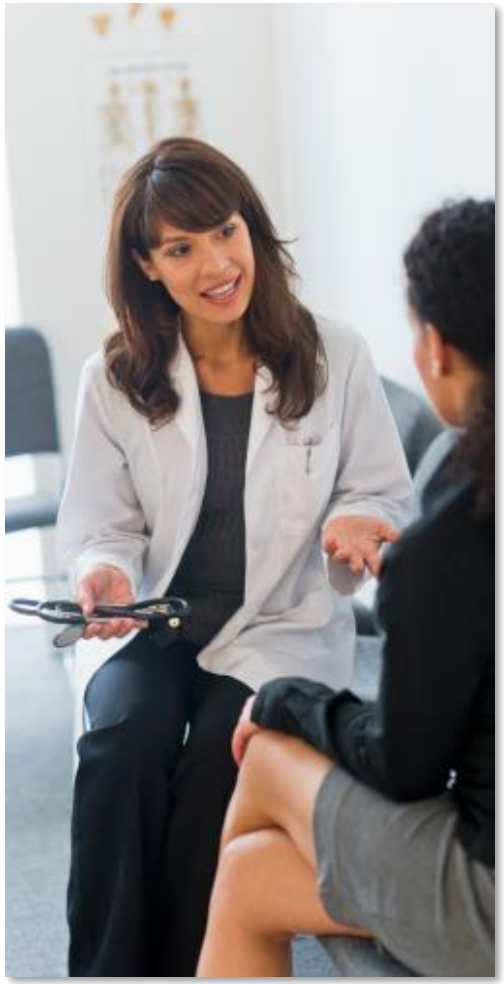
February 3, 2020

One Quality Voice for Patients



We Are Patients, Too.

MAY 4 – JUNE 7, 2018



Consumer Knowledge of Drug Quality

FDABAA-16-00122

HHSF223201710128C

SEPT 25 – OCT 9, 2018

Physician Knowledge of Drug Quality

FDABAA-16-00122

HHSF223201710128C

Respondents

Consumers

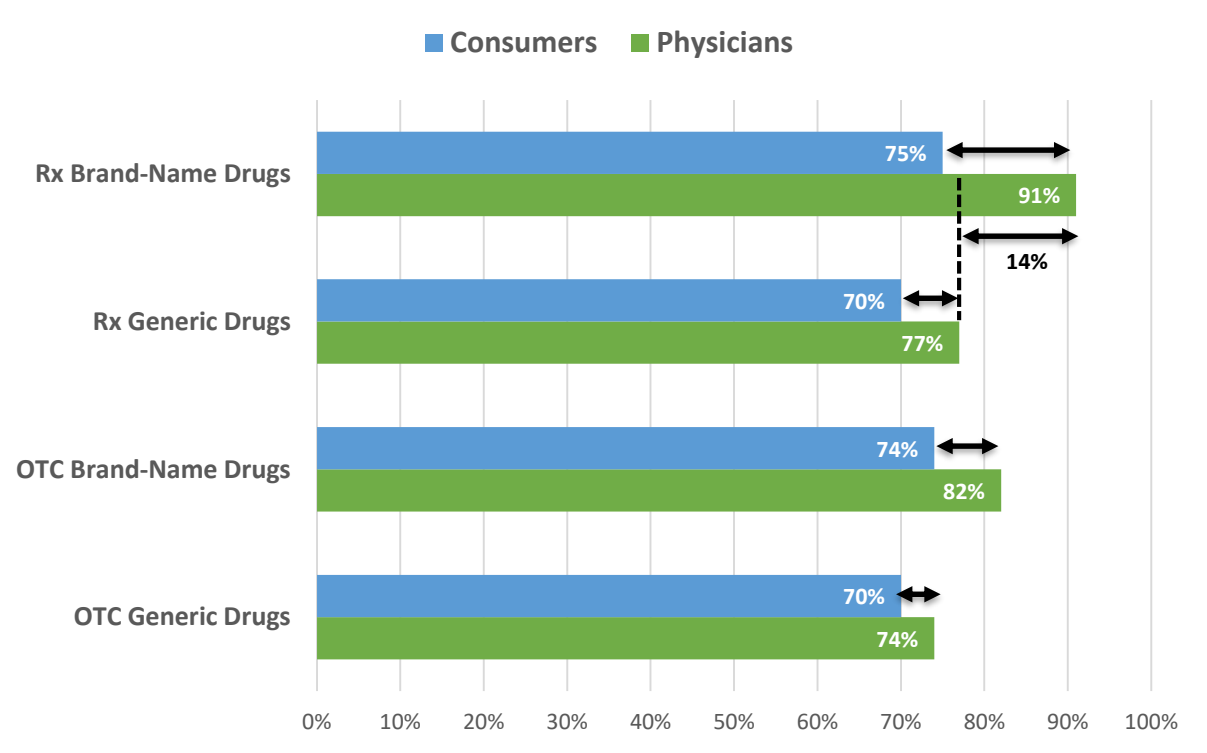
- **3,037 WebMD site visitors**
  - Desktop & Mobile
- **62% Age <50 Years**
- **12.5% Hispanic**
- **14.4% Black**

Physicians

- **650 Physicians from Email Invite**
  - Age >26, 5 years post-residency, >40% direct patient care, etc.
  - $25-50 Amazon Gift Card
- **61.5% Primary Care Physicians**
- **55% >15 Years in Practice**
- **7.7% Each:**
  - Cardiologists
  - Dermatologists
  - Endocrinologists
  - Orthopedics
  - Rheumatologists

Overall Perceptions of Drug Quality

The overall quality of […] drugs… is very good/excellent



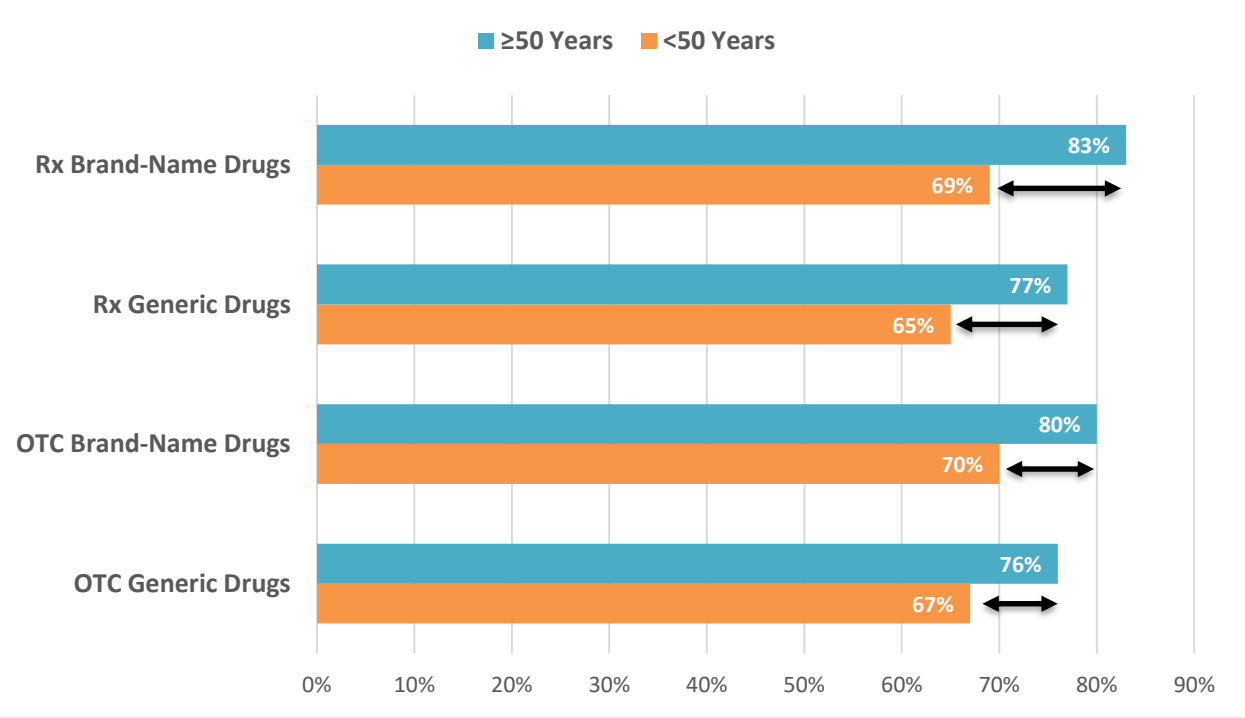
- Physician ratings for drug quality were higher compared to consumers
- Physicians had more tendency to associate brand-name drugs with superior quality than generics

Base: Total respondents

Age & Perceptions of Drug Quality

Consumers:

The overall quality of […] drugs… is very good/excellent

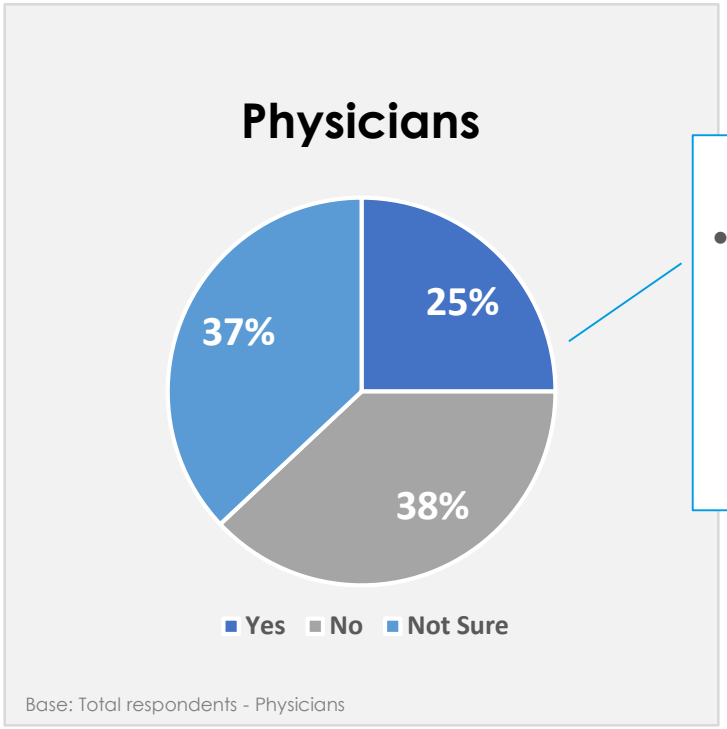


- Consumers age 50 or over are more likely to rate drug quality as very good or excellent as compared to those <50
- The younger cohort was more likely to give a good or fair rating

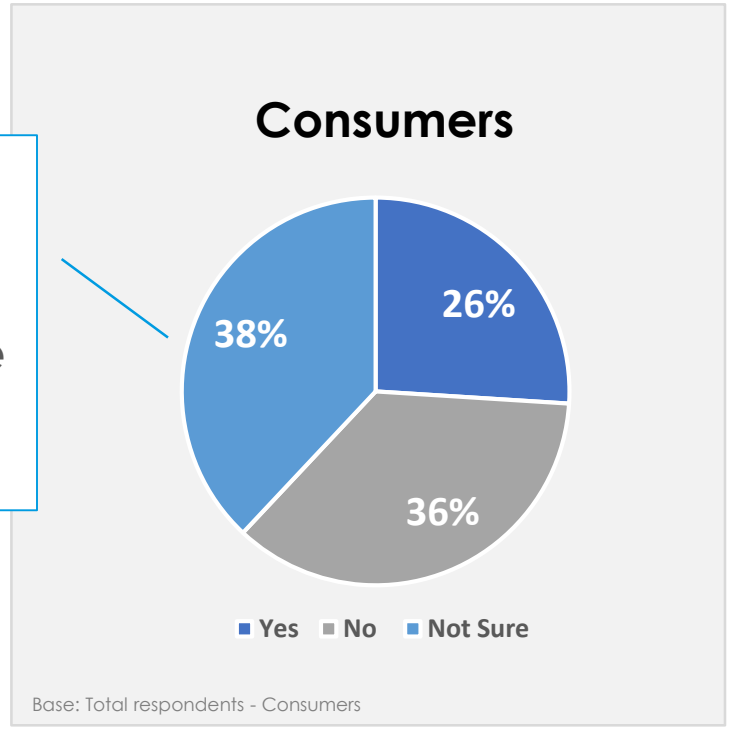
Base: Total respondents - Consumers

Perceptions of Drug Manufacturing

Do you believe drugs manufactured outside the U.S. and sold in the U.S. adhere to strict manufacturing standards and regulations required by the FDA?

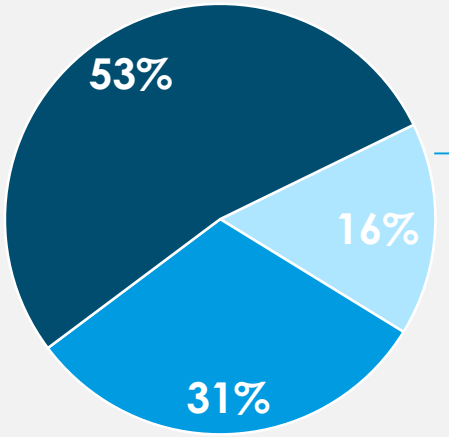


- Nearly three quarters of consumers AND physicians **do not believe** or **are not sure**



Frequency of Dispense as Written

Frequency of writing "DAW" for prescription brand-name drugs when a prescription generic is available



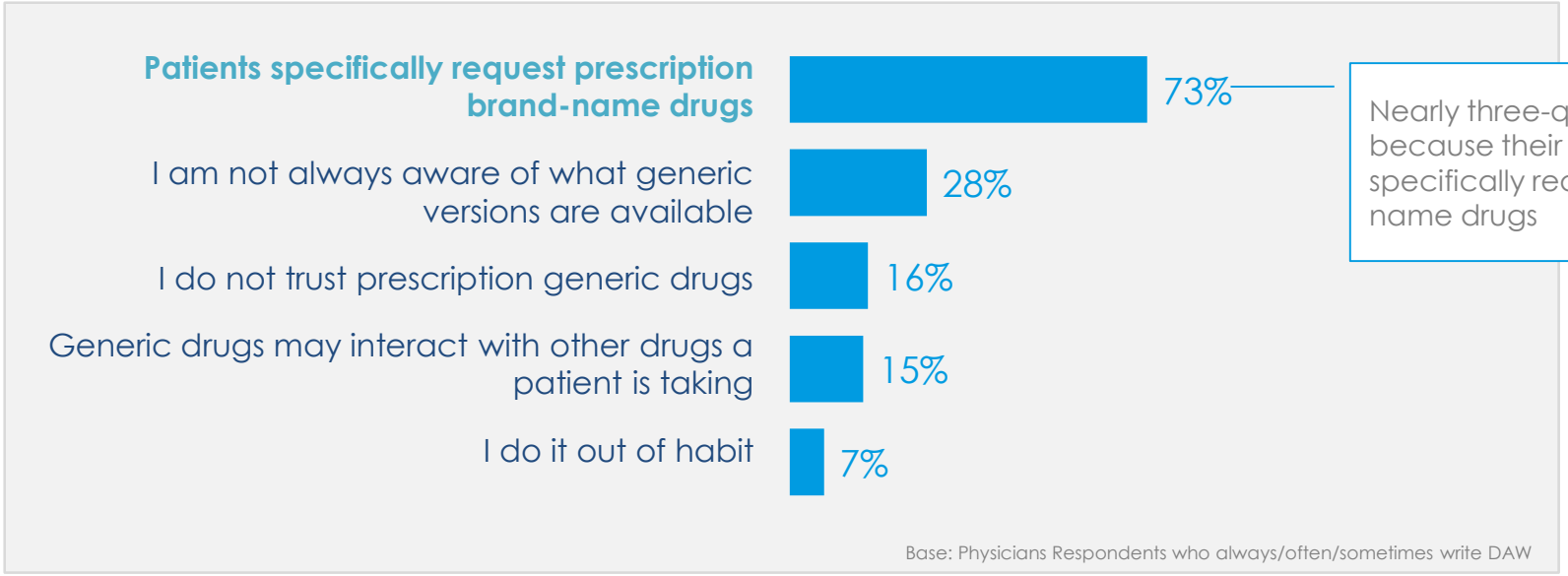
- Nearly half always/often/sometimes write DAW
- Significantly more specialists (21%) write DAW compared to PCPs (14%)
  - Highest among cardiologists (26%) and endocrinologists (28%)

Always/often Sometimes Rarely/Never

Base: Total respondents - Physicians

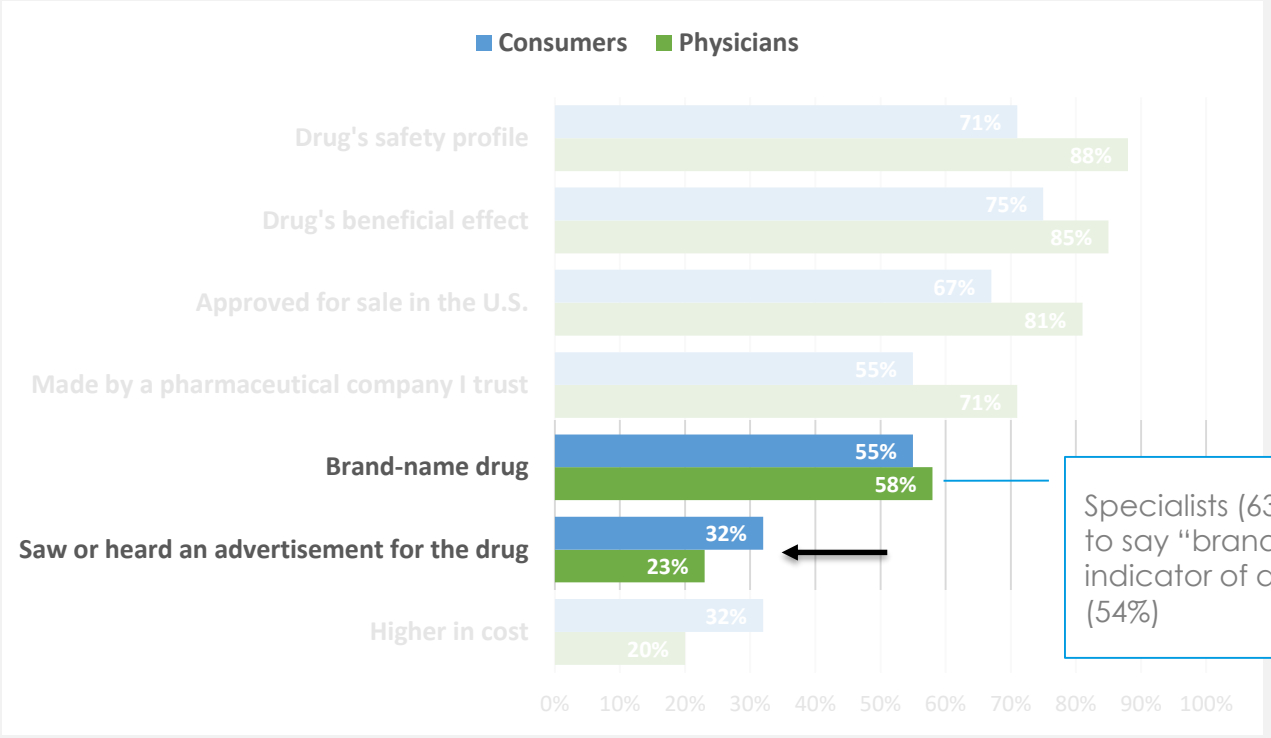
Reasons for Dispense as Written

Primary reasons for writing "DAW"



Factors Indicative of Drug Quality

Percentage Somewhat/Strongly Agree […] Is an Indicator of Drug Quality



- Nearly **one-quarter of physicians** and nearly **one-third of consumers** think advertising is an indicator of drug quality

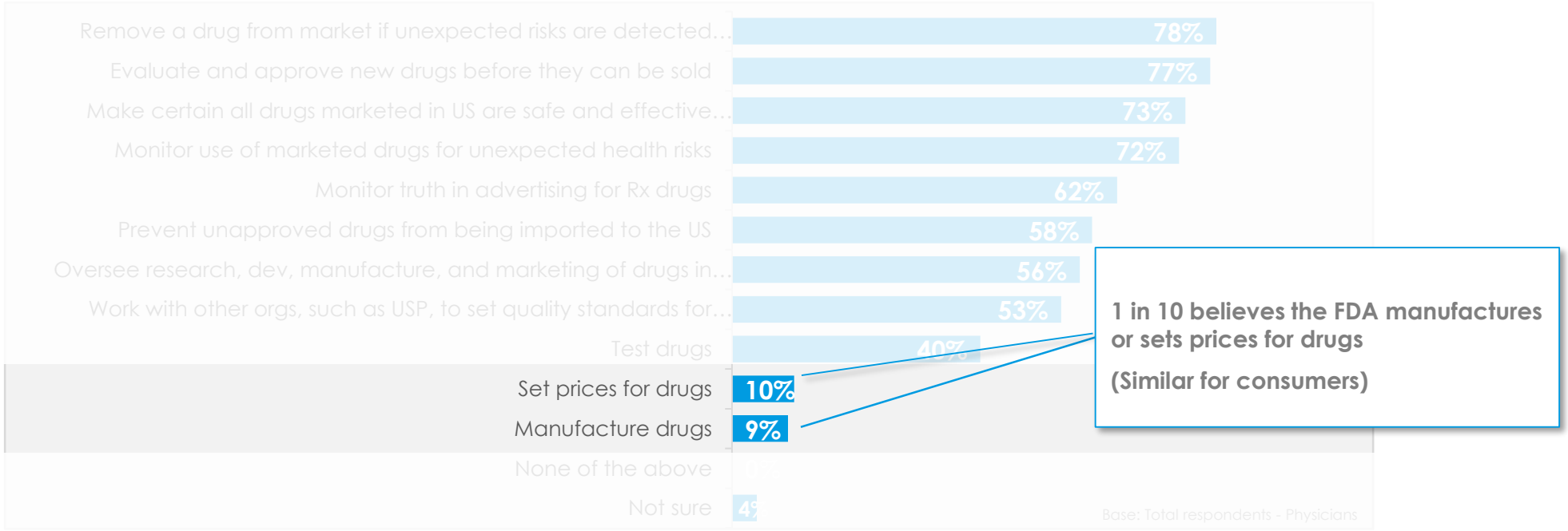
Specialists (63%) more likely to say "brand name" is an indicator of quality vs. PCPs (54%)

Base: Total respondents

FDA's Role in Regulating Drug Quality

Physicians:

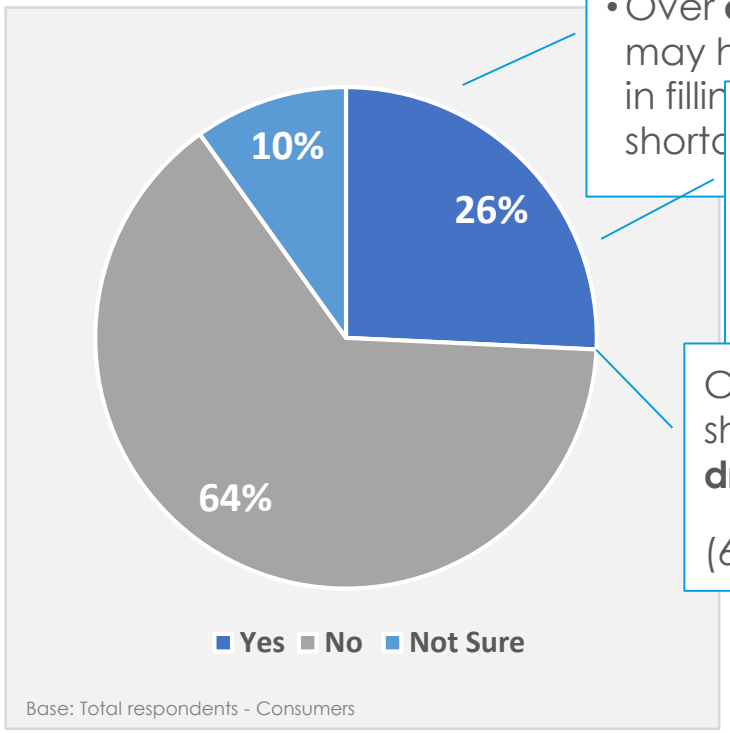
Which, if any, of the following are functions of the FDA in terms of regulating drug quality?



Drug Shortages

Consumers:

Have you experienced any difficulty in filling your prescription(s) due to drug shortage?



- Over **one-third** of consumers may have experienced difficulty in fillin
  shorta

Consumers who experienced a drug shortage were more likely to have used an **Rx generic drug** in the past 3 years

(88% vs. 68% Rx Brand)

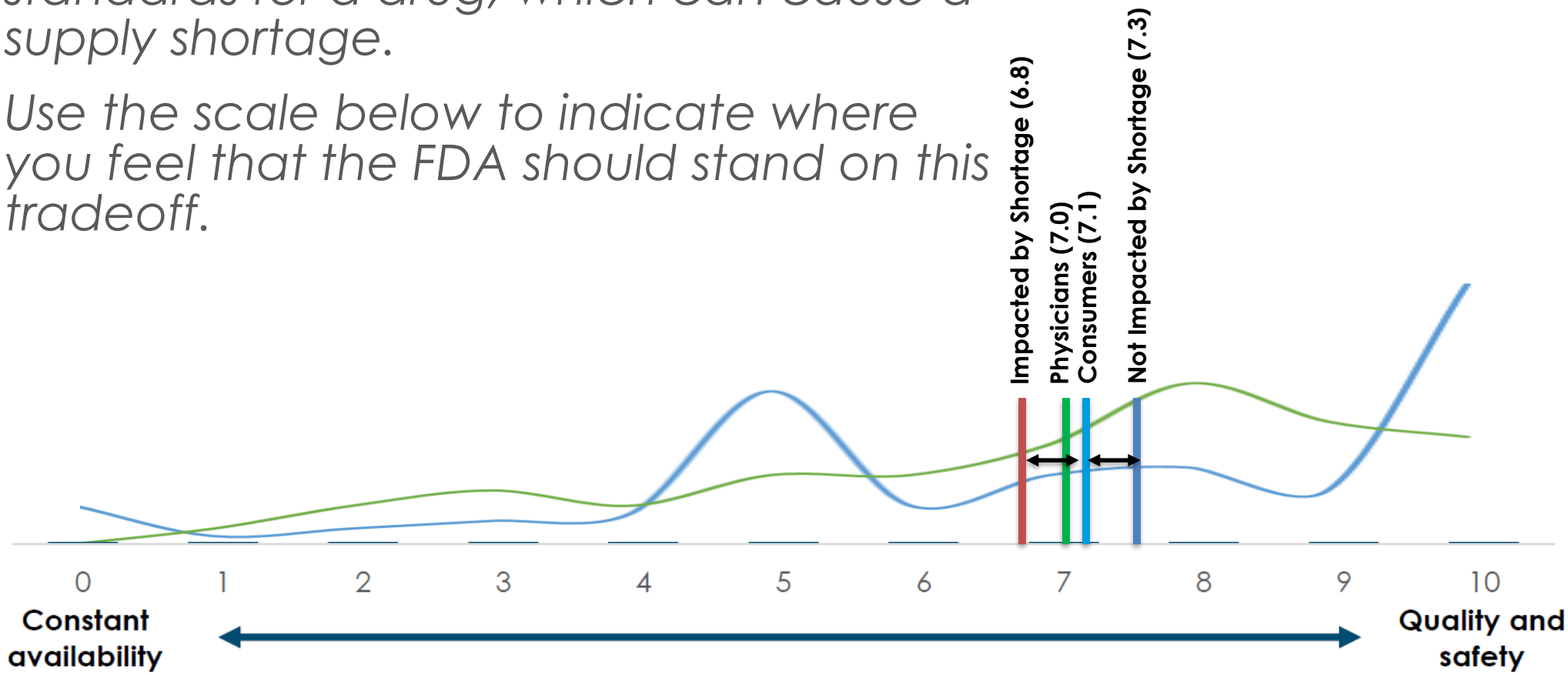
Consumers who experienced drug shortages tended to rate **Rx generic drug quality** lower

(64% vs. 73% very good/excellent)

Constant Availability vs. Quality

There are times when the FDA may take steps to maintain safety and quality standards for a drug, which can cause a supply shortage.

Use the scale below to indicate where you feel that the FDA should stand on this tradeoff.



Key Takeaways

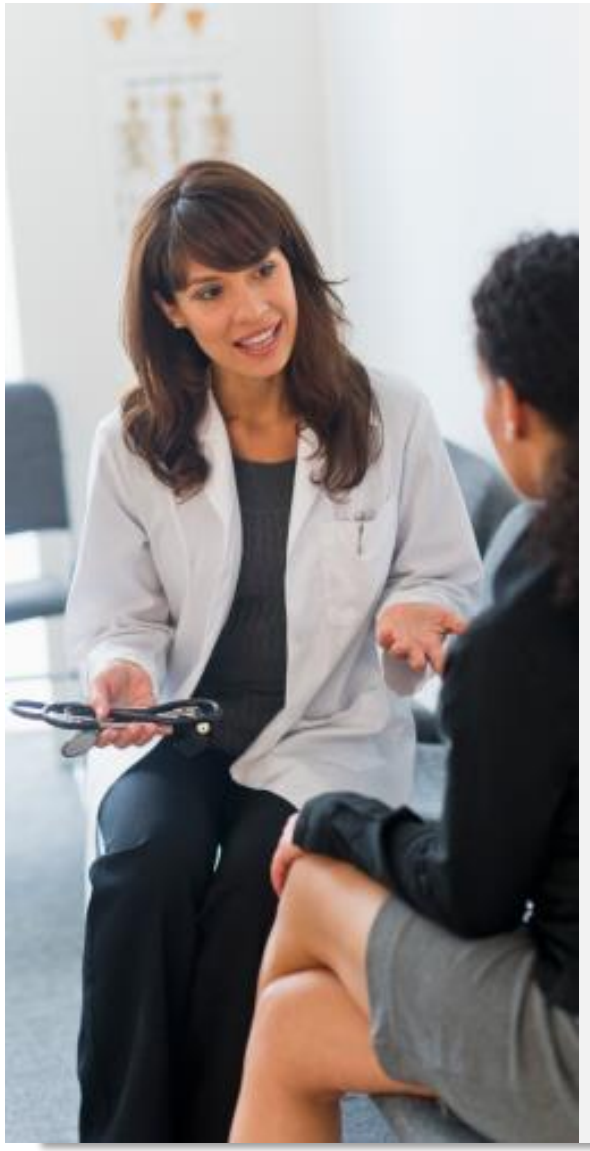
Consumers

- Three-quarters are uncertain that drugs manufactured abroad adhere to FDA's quality standards
- Most, but not all, knew the FDA neither manufactures drugs nor sets drug prices
- Experiences with shortages influence perceptions of quality

Physicians

- Half believe drugs manufactured abroad are of lower quality
- One-quarter believe a drug advertisement is an indicator of a quality
- Half sometimes or often write DAW
- Three-quarters do this because patients request them to

Key Takeaways



To maintain confidence in medicine, there is an opportunity for FDA to better understand stakeholder sentiments

and to help facilitate conversations between physicians and patients about the quality of their drugs


FDA
U.S. FOOD & DRUG
ADMINISTRATION

The State of Pharmaceutical Quality

Closing Remarks

Adjournment

Thank You!

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