Surveillance Inspections and Recent Trends

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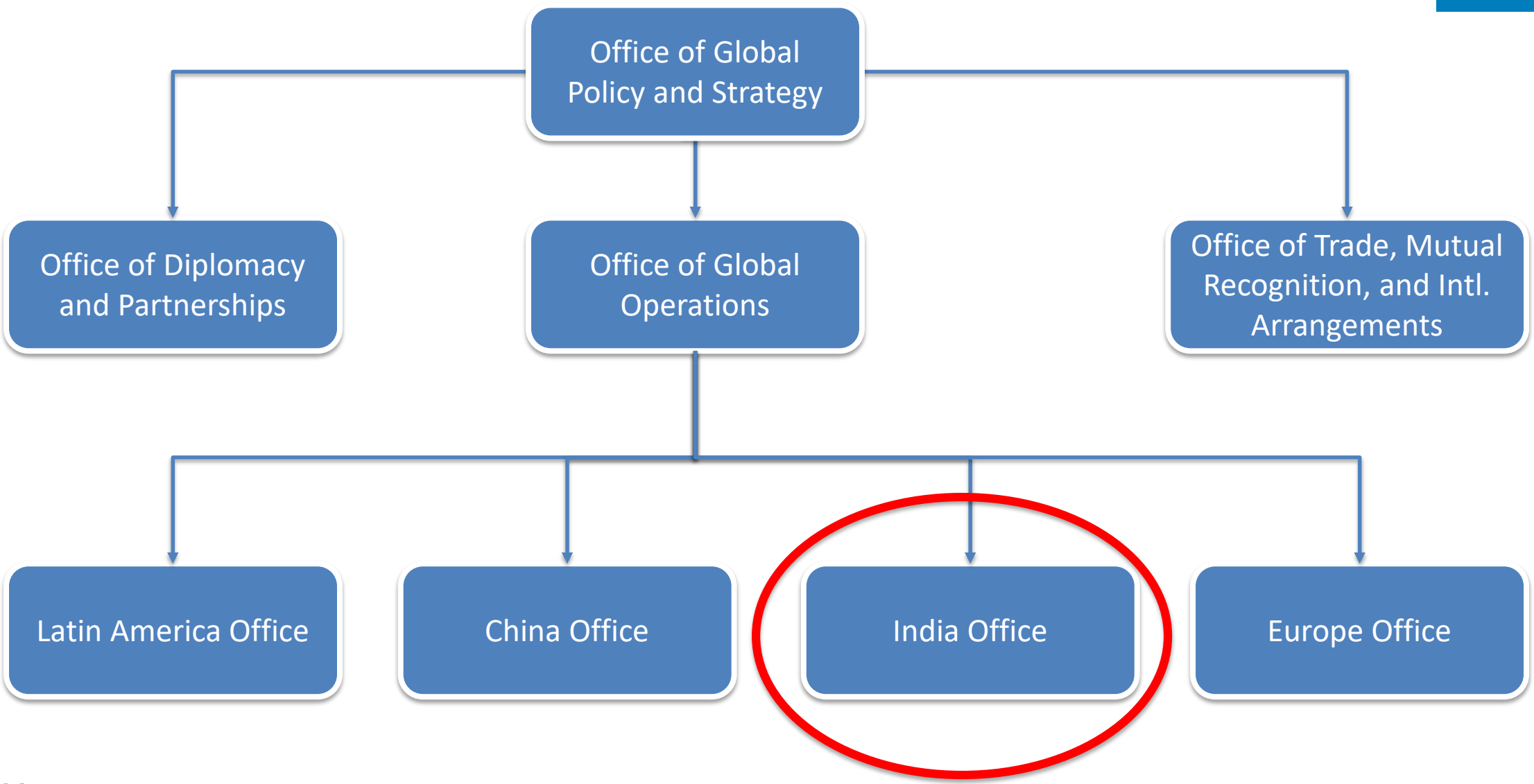
Agenda

- Office of Global Policy and Strategy
- Human Drug Inventory
- Site Selection Model (SSM)
- Concept of Operations (ConOps)
- Inspection Trends

Office of Global Policy and Strategy



Office of Global Policy and Strategy

OGPS MISSION STATEMENT: OGPS works to protect and enhance the public health of Americans by ensuring that global considerations are fully integrated into the Agency's policies and operational activities.

STRATEGIC PRIORITY 1:
POLICY COHERENCE

Promote mutually reinforcing policy actions to advance FDA's public health and regulatory interests globally.

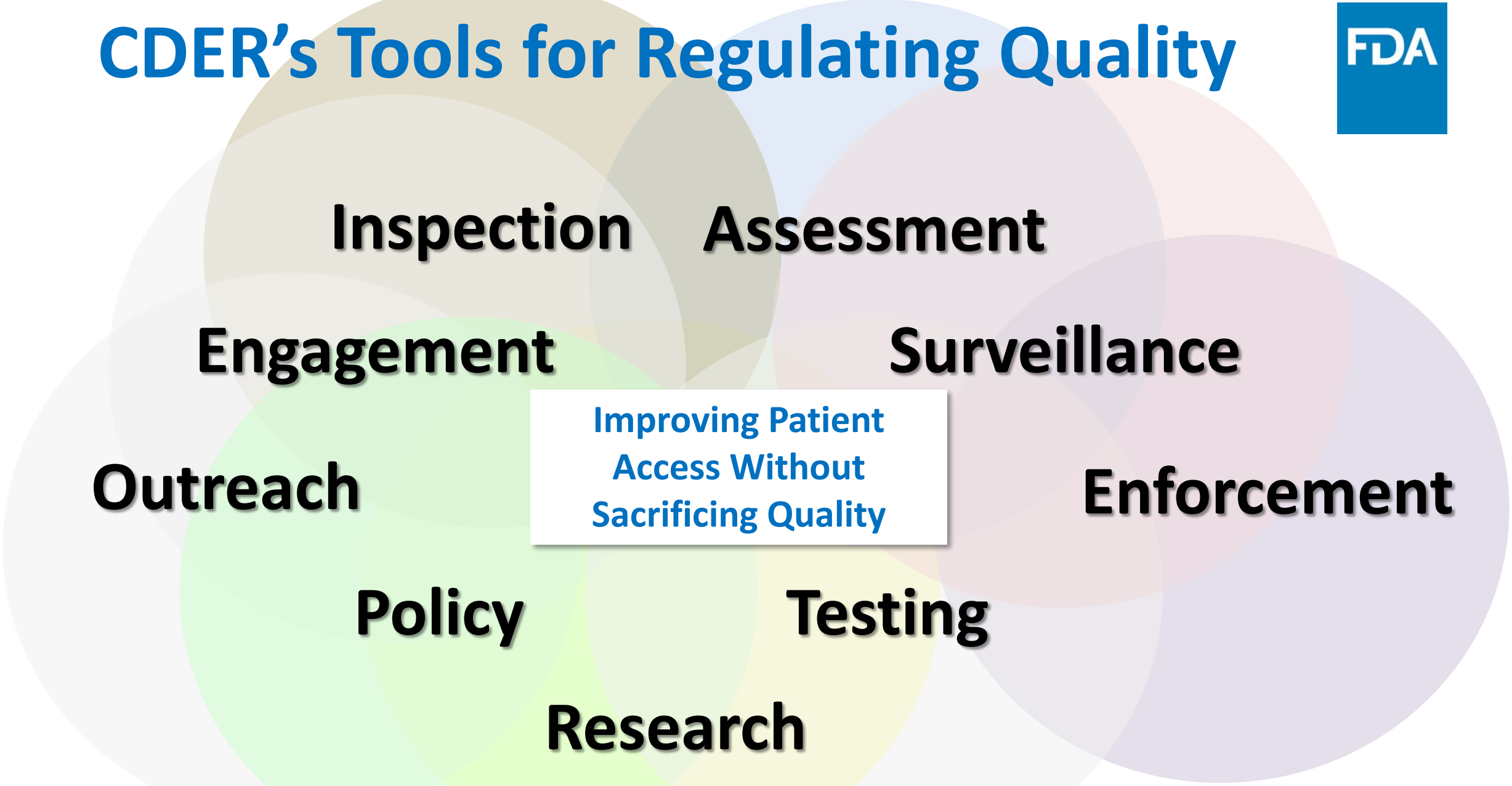
STRATEGIC PRIORITY 2:
GLOBAL PARTNERSHIPS

Build and leverage global partnerships to protect and promote public health.

STRATEGIC PRIORITY 3:
HIGH QUALITY INFORMATION

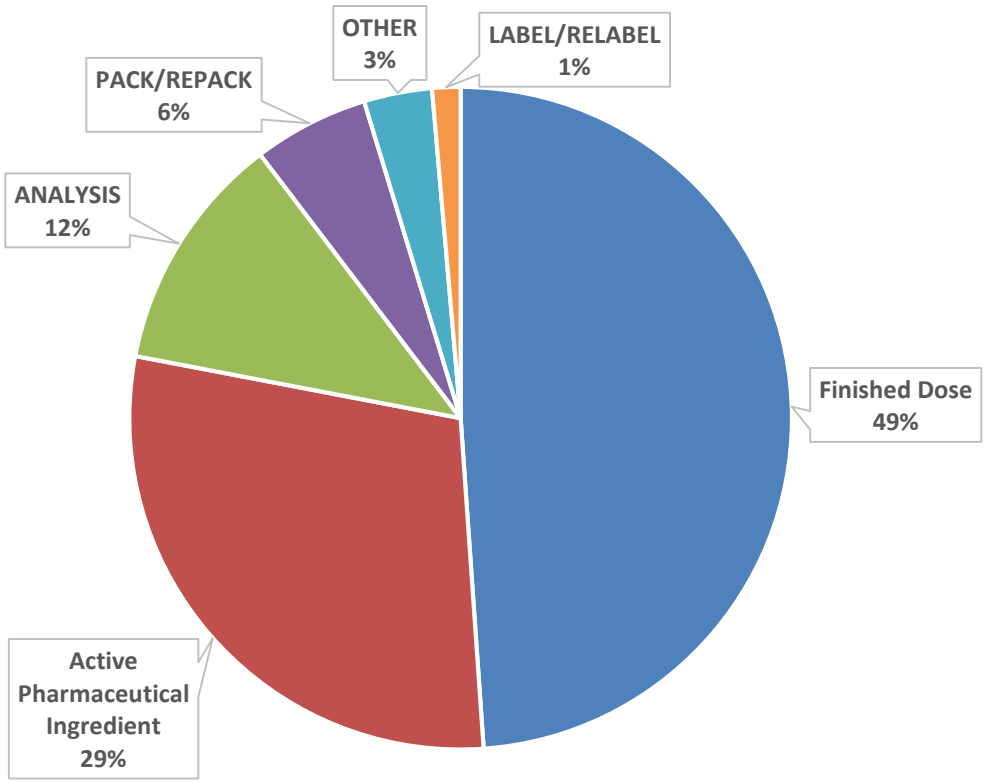
Collect, analyze, and share *high-quality* information, including inspections data, to advance FDA's public health mission.

CDER's Tools for Regulating Quality



Human Drug Inventory - Approximate Numbers

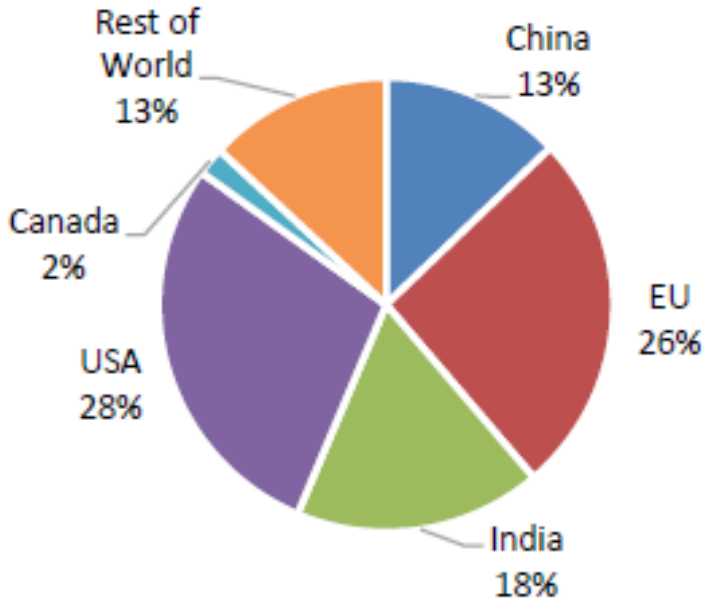
- Facilities:
  - ~6,000 human drug manufacturing sites
  - ~2,000 Medical Gas (MG) manufacturers (nearly all in U.S.)
  - ~4,000 Non-Medical Gas manufacturers
    - 44% domestic
    - 56% foreign
- Products:
  - 120,000 unique finished dose
  - 35,000 unique Active Pharmaceutical Ingredients
- Foreign : ~2200 Sites
  - India: 476 sites
  - China: 347 sites
  - Rest of the World: 1455 sites



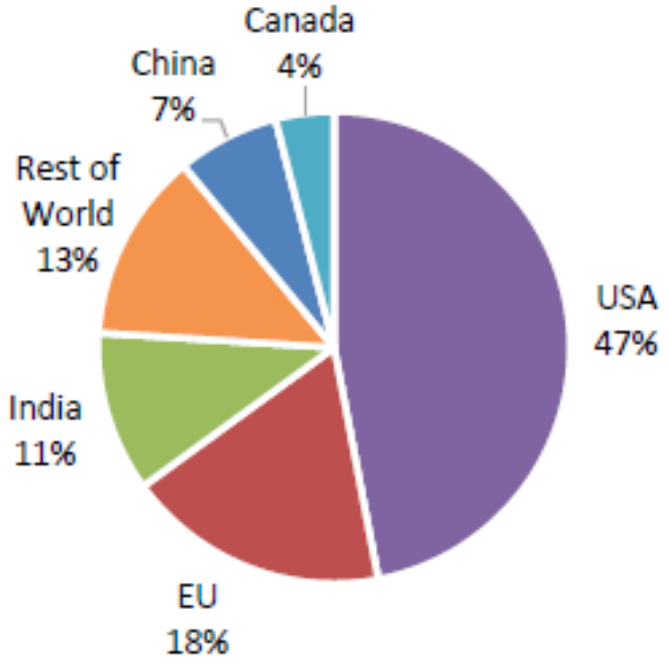
- The hierarchy for this analysis tags a site that makes both FDF and API as FDF facilities and a facility that makes both application and non application products as an application site.
- ***Note:*** *Based on July 2019 Surveillance Catalogs and current eDRLS listings.*

Human Drug Inventory - Approximate Numbers

Percentage of Active Pharmacetical Ingredient Manufacturing Facilities for All Drugs by Country or Region, August 2019



Percentage of Finished Dosage Form Manufacturing Facilities for All Drugs by Country or Region, August 2019

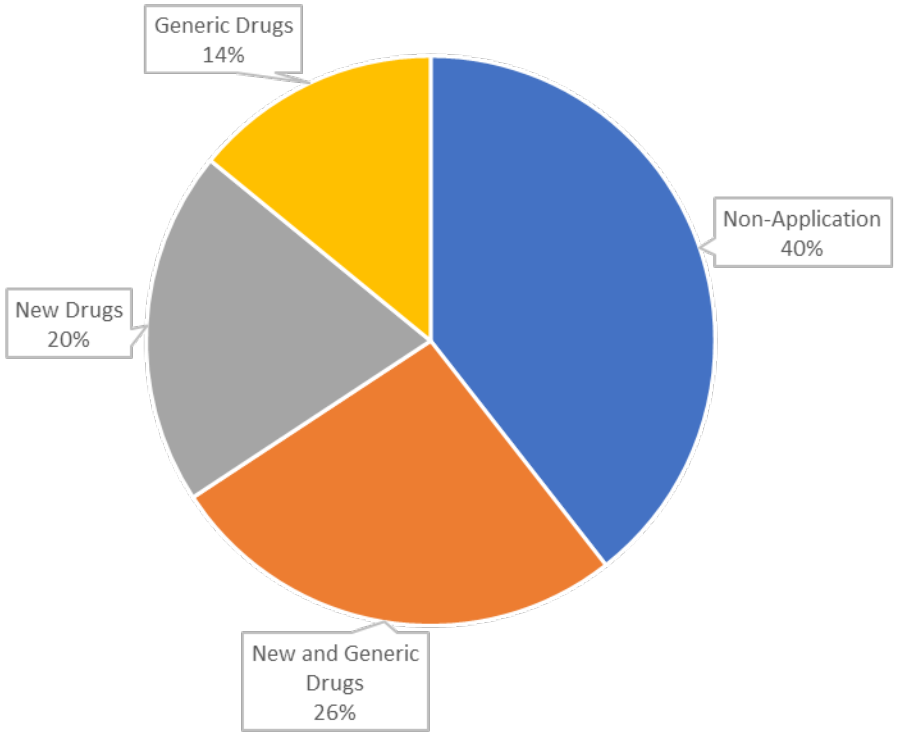


Human Drug Inventory - Approximate Numbers

- 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)

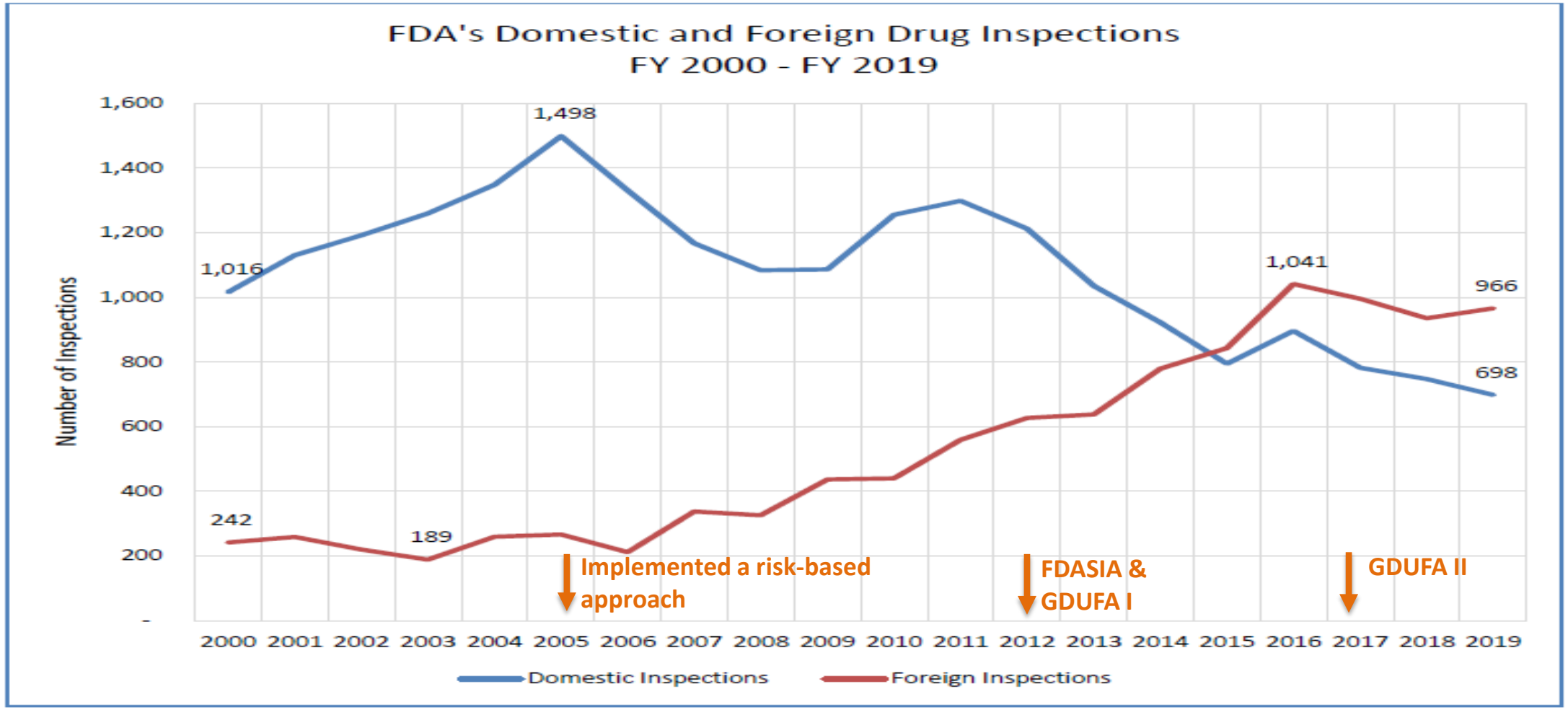
- **60% of all facilities are listed in application products**

- **40% of all facilities manufacture non-application products**

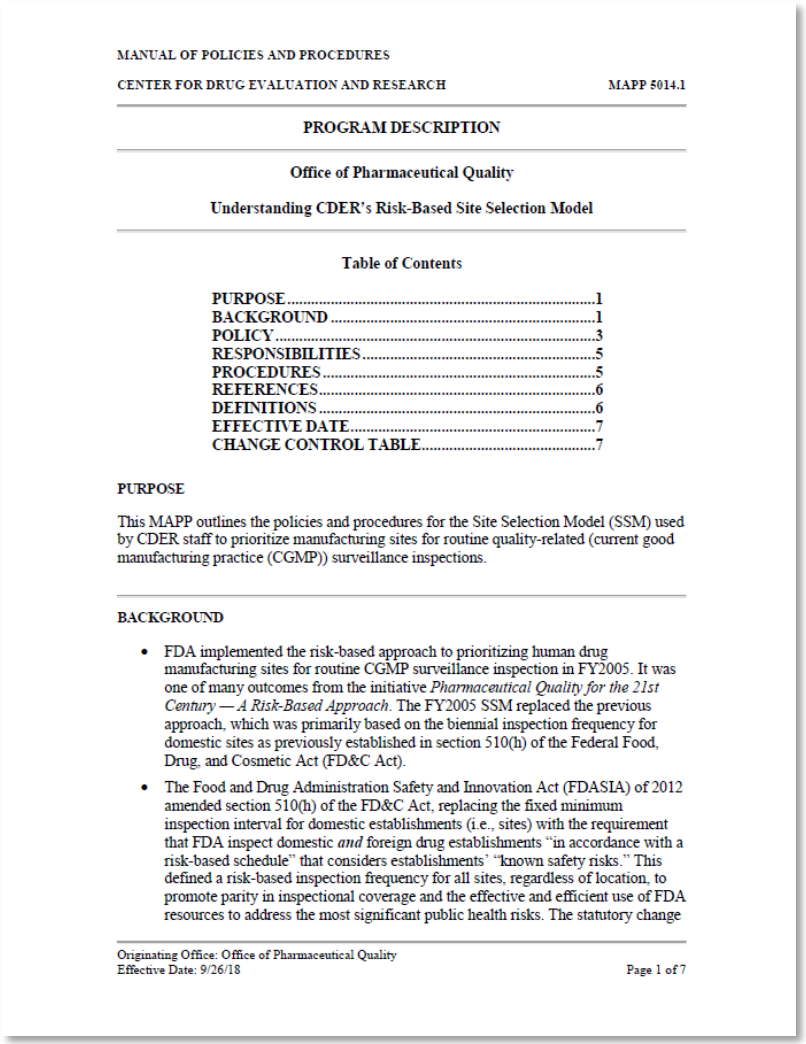


* Medical Gas not included

FDA's Domestic and Foreign Drug Inspections (FY2000 – FY2019)



CDER-ORA Site Selection Model (SSM)



MANUAL OF POLICIES AND PROCEDURES

CENTER FOR DRUG EVALUATION AND RESEARCH MAPP 5014.1

PROGRAM DESCRIPTION

Office of Pharmaceutical Quality

Understanding CDER's Risk-Based Site Selection Model

Table of Contents

PURPOSE

This MAPP outlines the policies and procedures for the Site Selection Model (SSM) used by CDER staff to prioritize manufacturing sites for routine quality-related (current good manufacturing practice (CGMP)) surveillance inspections.

BACKGROUND

- FDA implemented the risk-based approach to prioritizing human drug manufacturing sites for routine CGMP surveillance inspection in FY2005. It was one of many outcomes from the initiative *Pharmaceutical Quality for the 21st Century — A Risk-Based Approach*. The FY2005 SSM replaced the previous approach, which was primarily based on the biennial inspection frequency for domestic sites as previously established in section 510(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).
- The Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 amended section 510(h) of the FD&C Act, replacing the fixed minimum inspection interval for domestic establishments (i.e., sites) with the requirement that FDA inspect domestic *and* foreign drug establishments "in accordance with a risk-based schedule" that considers establishments' "known safety risks." This defined a risk-based inspection frequency for all sites, regardless of location, to promote parity in inspectional coverage and the effective and efficient use of FDA resources to address the most significant public health risks. The statutory change

Originating Office: Office of Pharmaceutical Quality
Effective Date: 9/26/18 Page 1 of 7

Sources of Information for Quality Surveillance

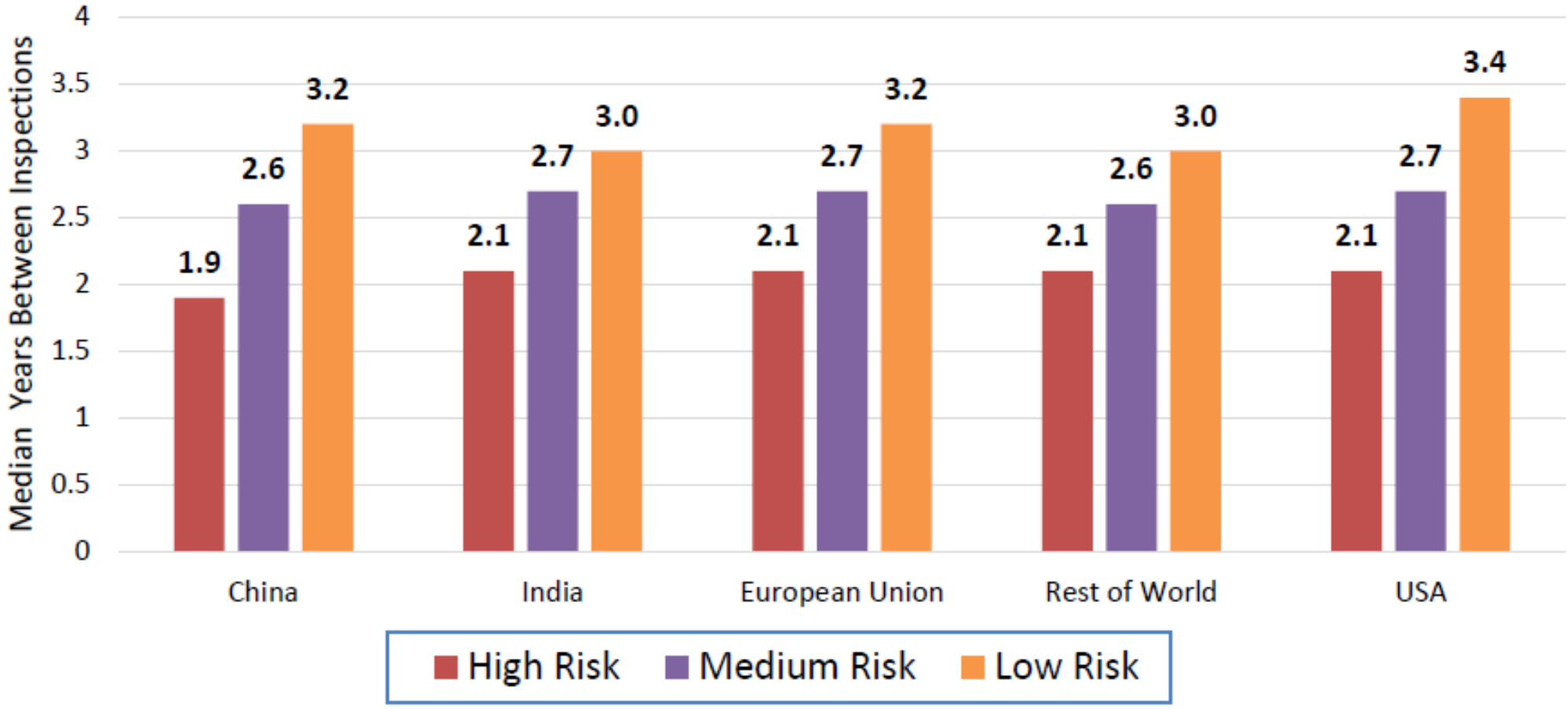
- Inherent Product Risk
- Facility Type
- Patient Exposure

Fairly Static

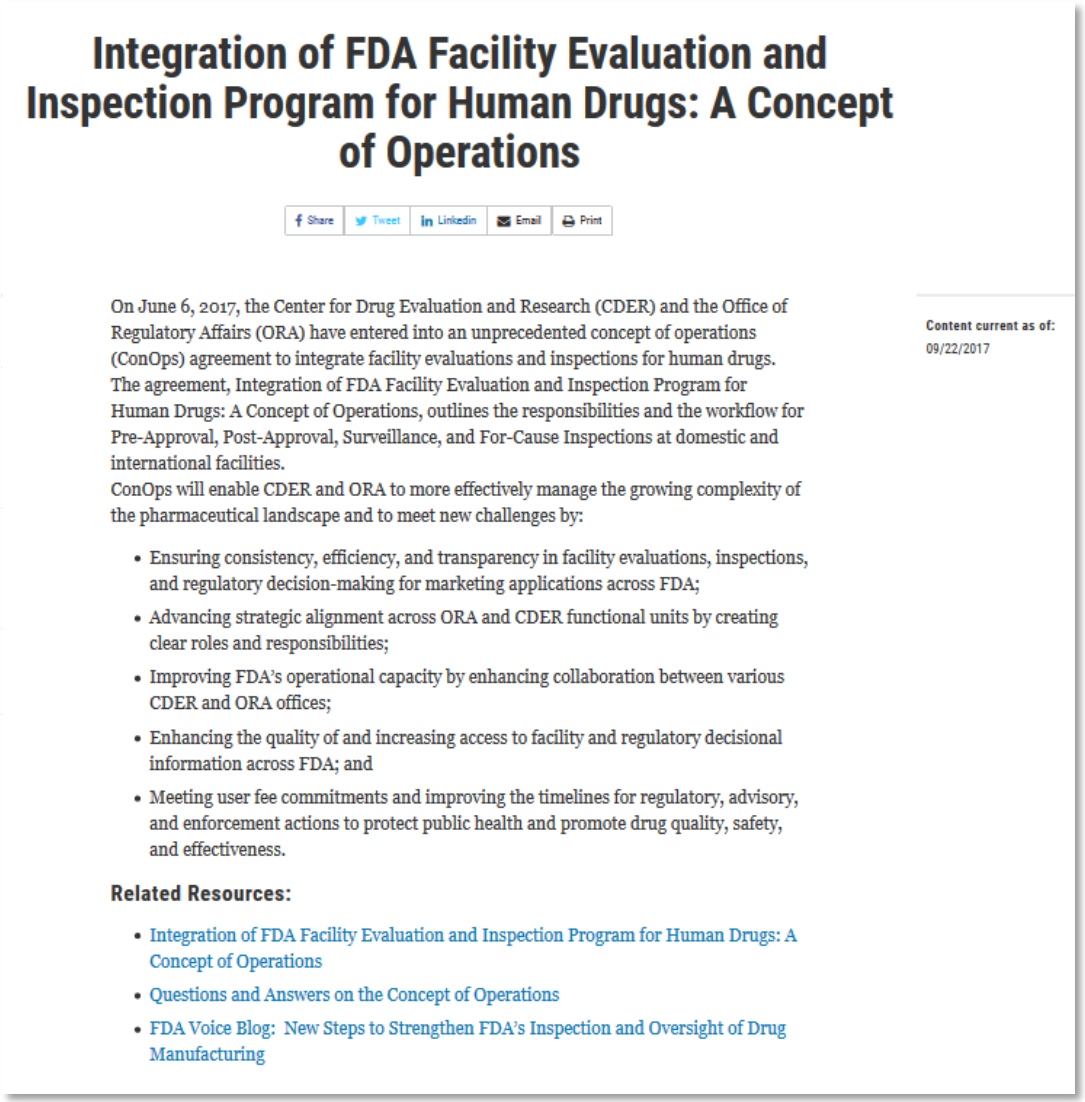
- Inspection History
- Time Since Last Inspection
- Hazard Signals

Dynamic

Median Years Between Drug Inspections By Risk Level (December 2011 – June 2019)



Concept of Operations (ConOps)



Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations

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Content current as of: 09/22/2017

On June 6, 2017, the Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA) have entered into an unprecedented concept of operations (ConOps) agreement to integrate facility evaluations and inspections for human drugs. The agreement, Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations, outlines the responsibilities and the workflow for Pre-Approval, Post-Approval, Surveillance, and For-Cause Inspections at domestic and international facilities.

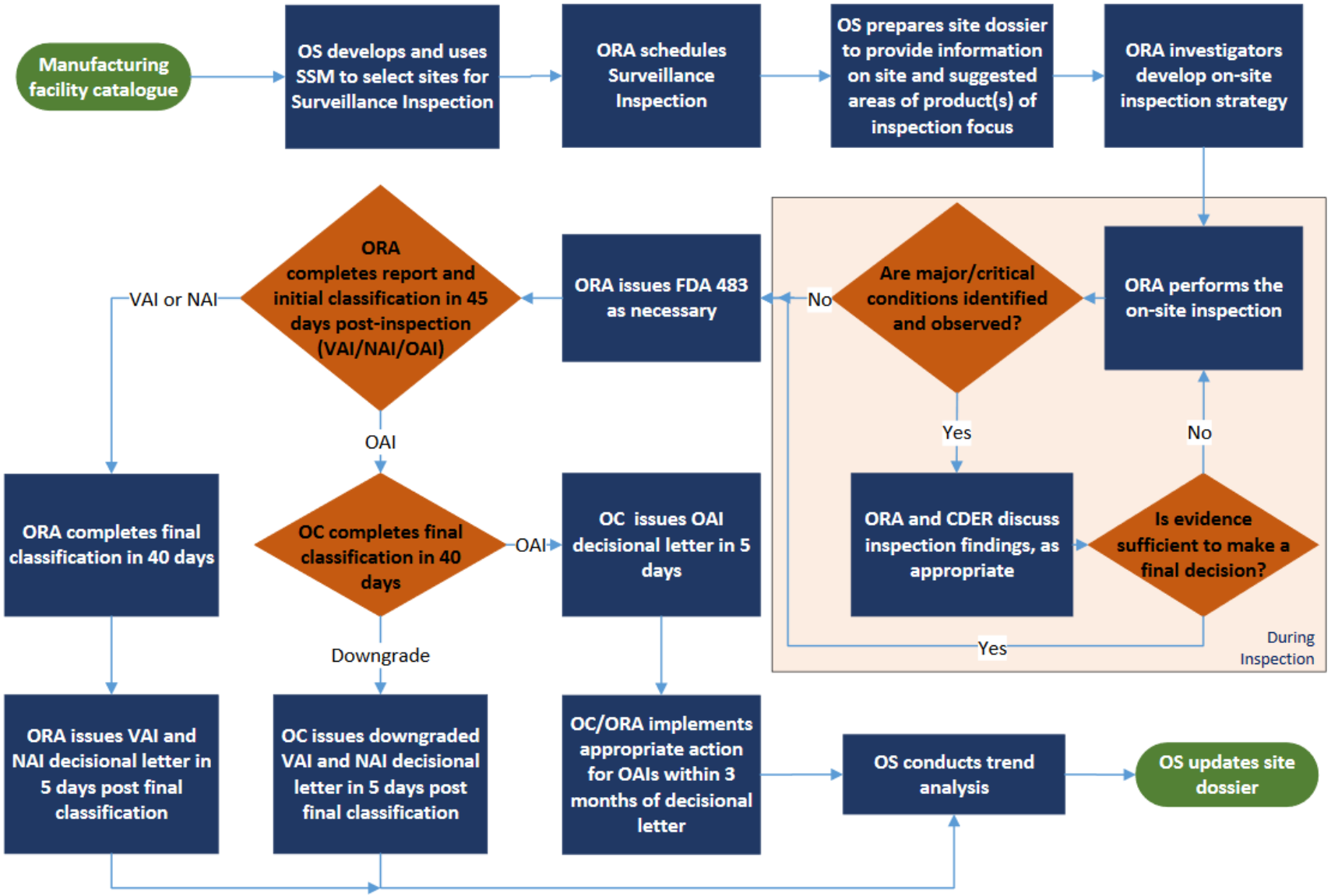
ConOps will enable CDER and ORA to more effectively manage the growing complexity of the pharmaceutical landscape and to meet new challenges by:

- Ensuring consistency, efficiency, and transparency in facility evaluations, inspections, and regulatory decision-making for marketing applications across FDA;
- Advancing strategic alignment across ORA and CDER functional units by creating clear roles and responsibilities;
- Improving FDA's operational capacity by enhancing collaboration between various CDER and ORA offices;
- Enhancing the quality of and increasing access to facility and regulatory decisional information across FDA; and
- Meeting user fee commitments and improving the timelines for regulatory, advisory, and enforcement actions to protect public health and promote drug quality, safety, and effectiveness.

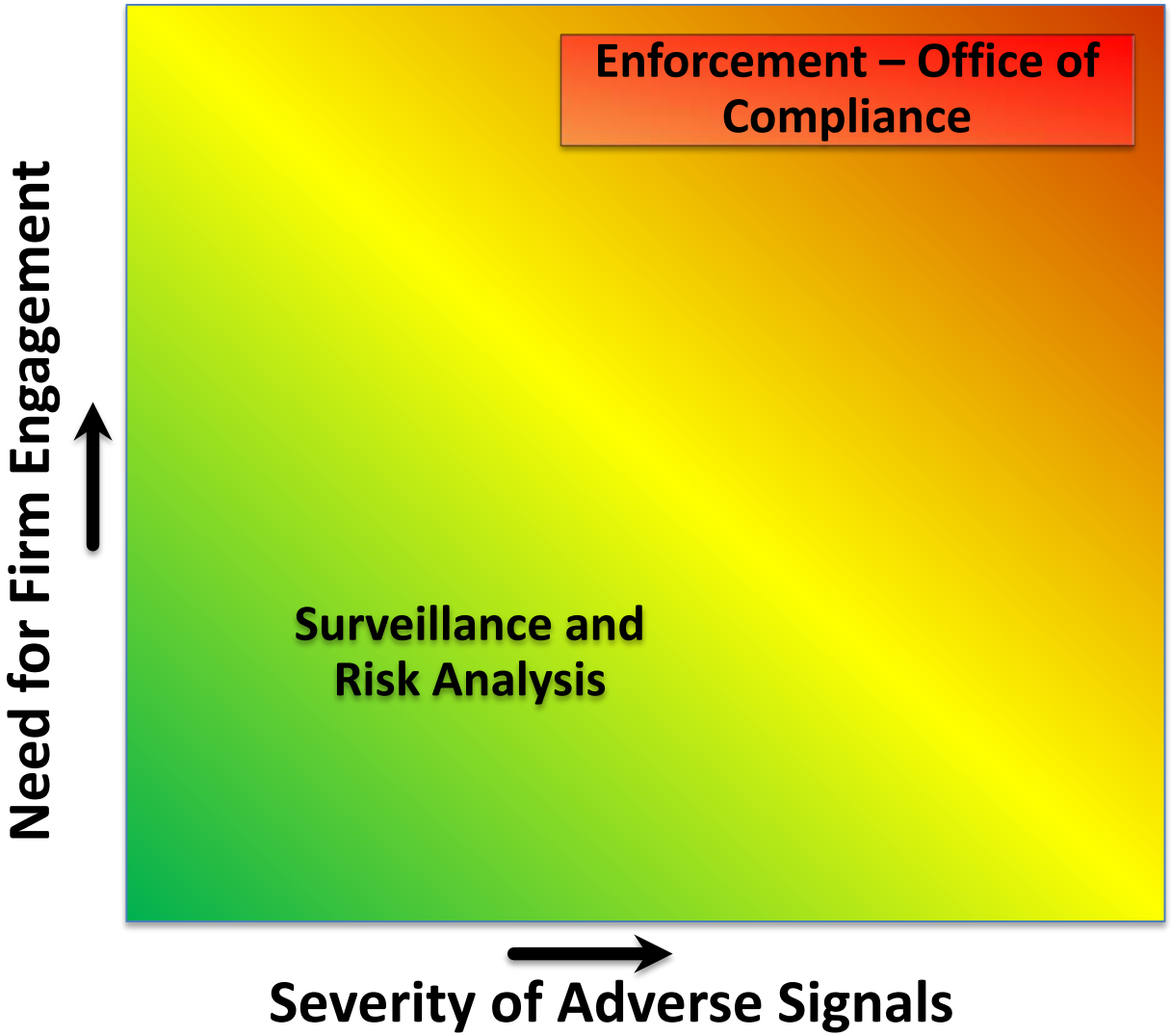
Related Resources:

- Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations
- Questions and Answers on the Concept of Operations
- FDA Voice Blog: New Steps to Strengthen FDA's Inspection and Oversight of Drug Manufacturing

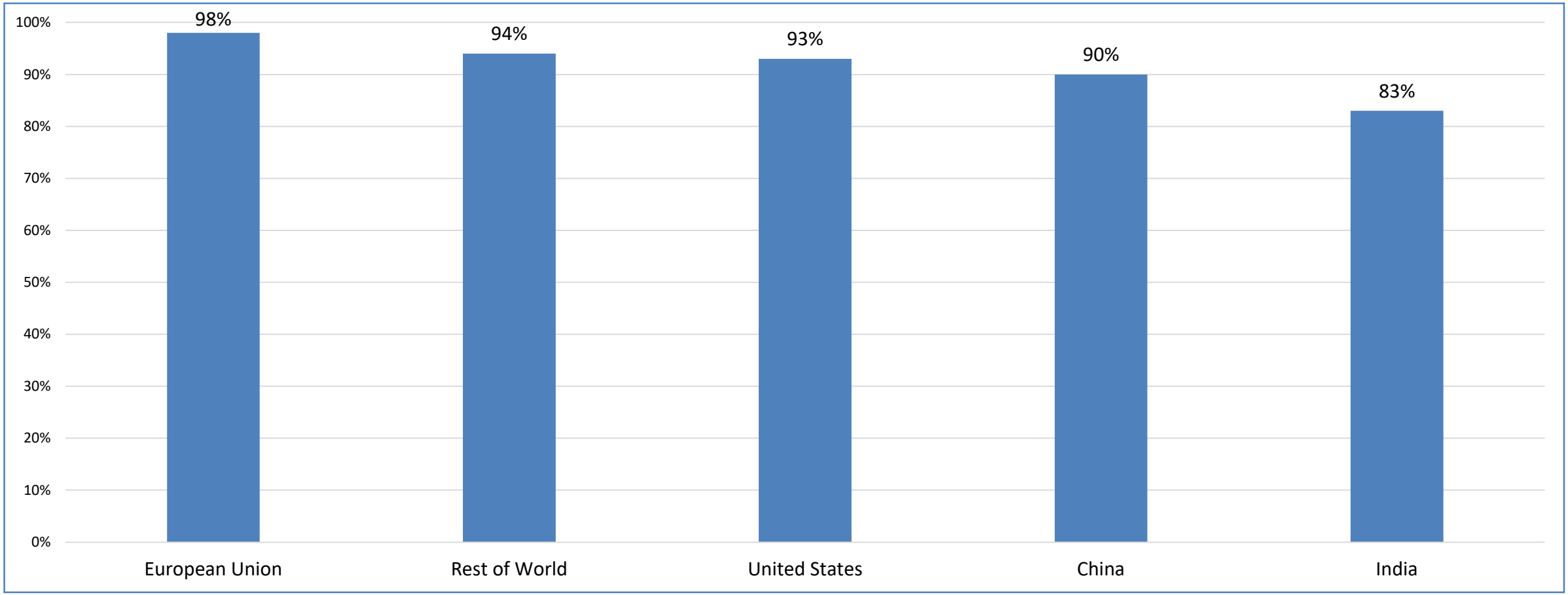
ConOps – Surveillance Facility Inspections



Surveillance vs Enforcement

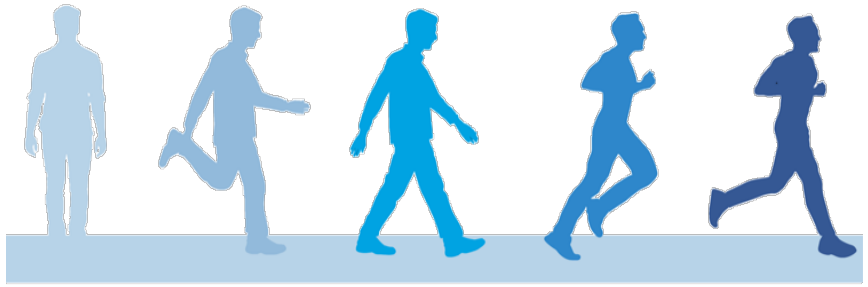


% of Manufacturing Facilities with Acceptable Final Outcome (as of August 2019)



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



Resources

- 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

Acknowledgements

- Office of Surveillance
- Office of Pharmaceutical Quality
- Office of Manufacturing Quality
- Office of Regulatory Affairs

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