Pharmaceutical Quality Surveillance Program

Cindy Buhse
Director, Office of Quality Surveillance
FDA/CDER/OPQ
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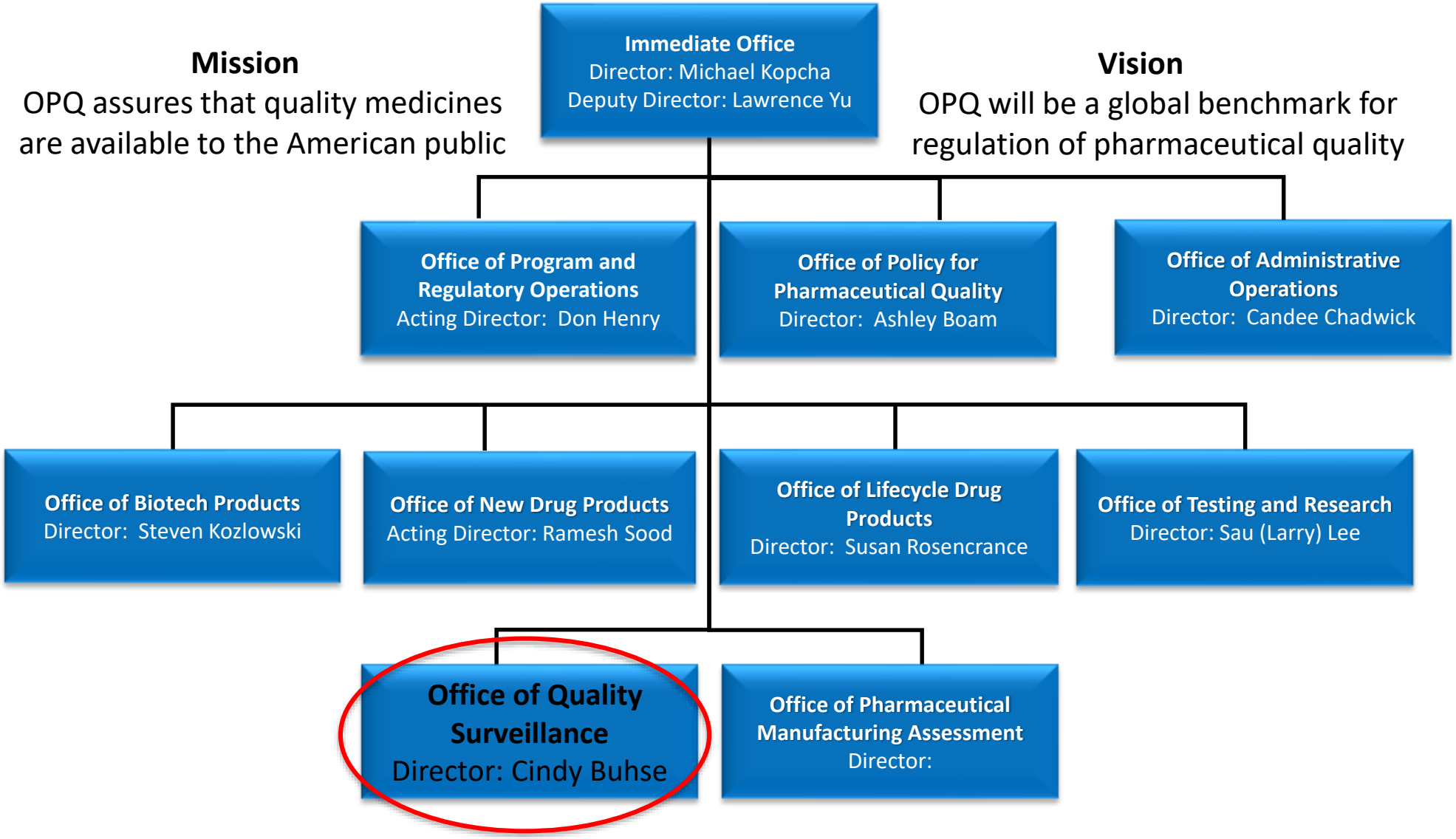
Learning Objectives

- Understand FDA's pharmaceutical quality surveillance program
- Learn various data sources FDA uses for post-marketing surveillance activities

The Office of Pharmaceutical Quality

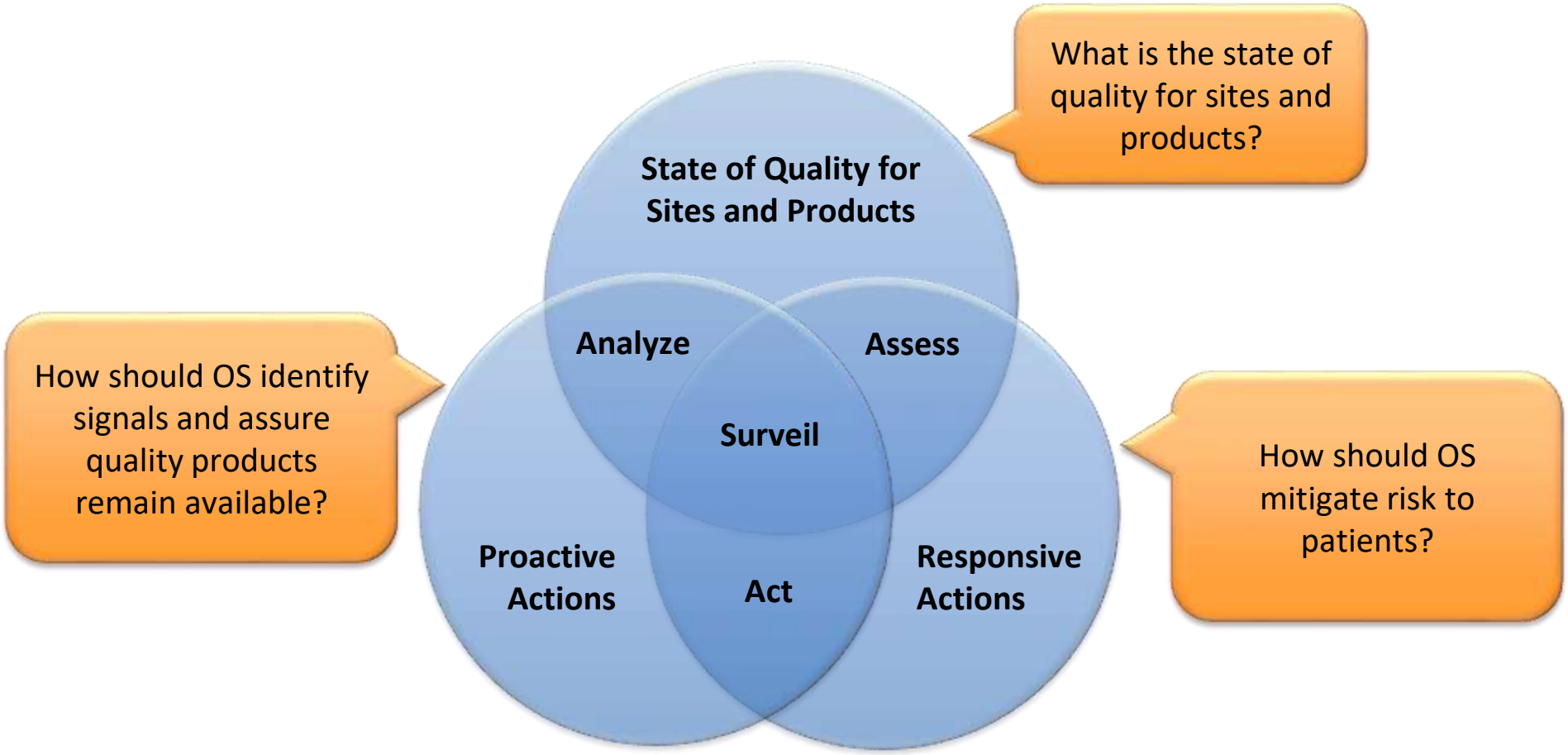
Mission
OPQ assures that quality medicines are available to the American public

Vision
OPQ will be a global benchmark for regulation of pharmaceutical quality



CDER/OPQ'S Office of Quality Surveillance

Office of Quality Surveillance



Human Drug Inventory by Approximate Numbers

Sites:

- ~6,000 human drug manufacturing sites of obligation (as defined by regulations and policy)
  - ~2,000 Medical Gas (MG) manufacturers (nearly all in U.S.)
  - ~4,000 Non-MG manufacturers
    - 44% domestic
    - 56% foreign

Products:

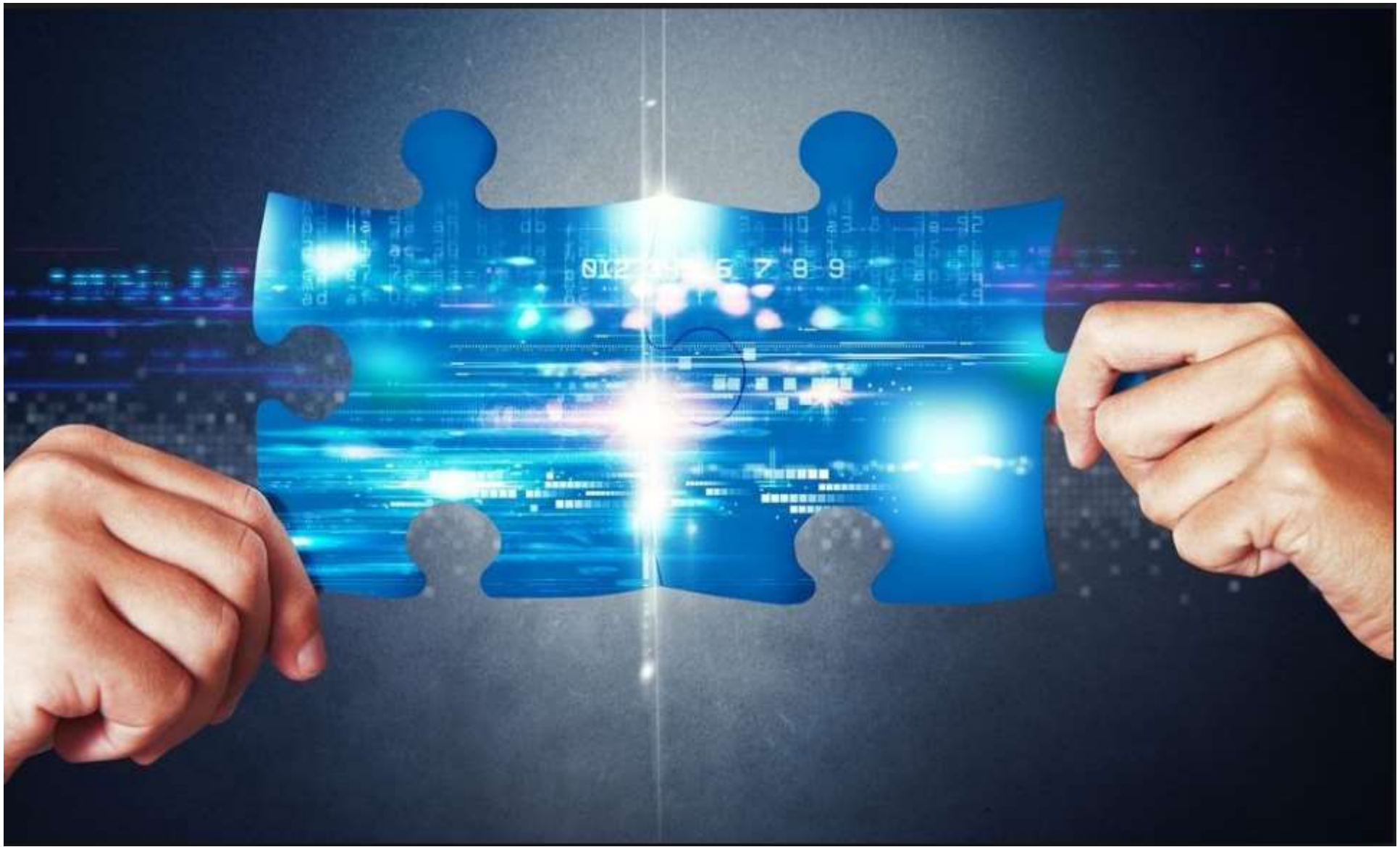
- 120,000 unique finished dose
- 35,000 unique APIs
- 800 unique medical gas

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

Sources of Information

- **Facility and Inspection Data**
  - Registration and Listing
  - Inspection findings
  - Profile Class Codes, Imports, Business operations, etc.
- **Quality Defect Reports**
  - Field Alert Reports (FARs)
  - MedWatch Reports
  - Biological Product Deviation Reports (BPDRs)
  - Recalls (Type I, II, III)
  - Consumer Complaints
- **Drug Quality Sampling and Testing Results**
- **Application data**
  - Original and Supplements
  - Annual Reports
- **Quality Metrics (future)**
- **External data**
  - Foreign regulatory authority information
  - Public information – social media, consumer reviews (e.g., drugs.com), blogs, news outlets, etc.

Turning Data into Intelligence



General Overview of Surveillance Activities

- Characterize the population of CDER-regulated sites and the products they manufacture
  - Prioritize sites and products for outreach after an emergency
- Monitor and quantitate the state of quality
  - Engage with pre-market review and compliance to enhance surveillance throughout the lifecycle
- Proactively identify potential quality signals and trends before serious quality problems occur

General Overview of Surveillance Activities (cont.)

- Use intelligence collected and analytics to make data-driven decisions that can reduce risk to patients
  - Prioritization of sites for CGMP inspections
  - Drug Quality Sampling and Testing Program
  - Site Dossier Program
  - **New Inspection Protocol Project**
  - **Site Engagement Program**
- Generate a Surveillance Action Plan that is comprehensive and uses resources most effectively
- Assess the effectiveness of a facilities Pharmaceutical Quality System (for established conditions, ICH-Q12)

Using Predictive Analytics to Be Proactive

- The use of data, statistical algorithms, and machine learning techniques to identify likelihood of future outcomes based on historical data
- Collaboration with Academia
  - St. Gallen University's Quality Metrics research grant – using predictive analytics (e.g., regression models) to help support the FDA program.
  - NIPTE grant – using analytics (e.g. web scraping, sentiment modeling) to enhance surveillance capabilities
  - Broad Agency Agreements
- Examples of Models:
  - Inspection outcome
  - Field Alert Report (FAR) models
  - Pharmaceutical Quality System Effectiveness

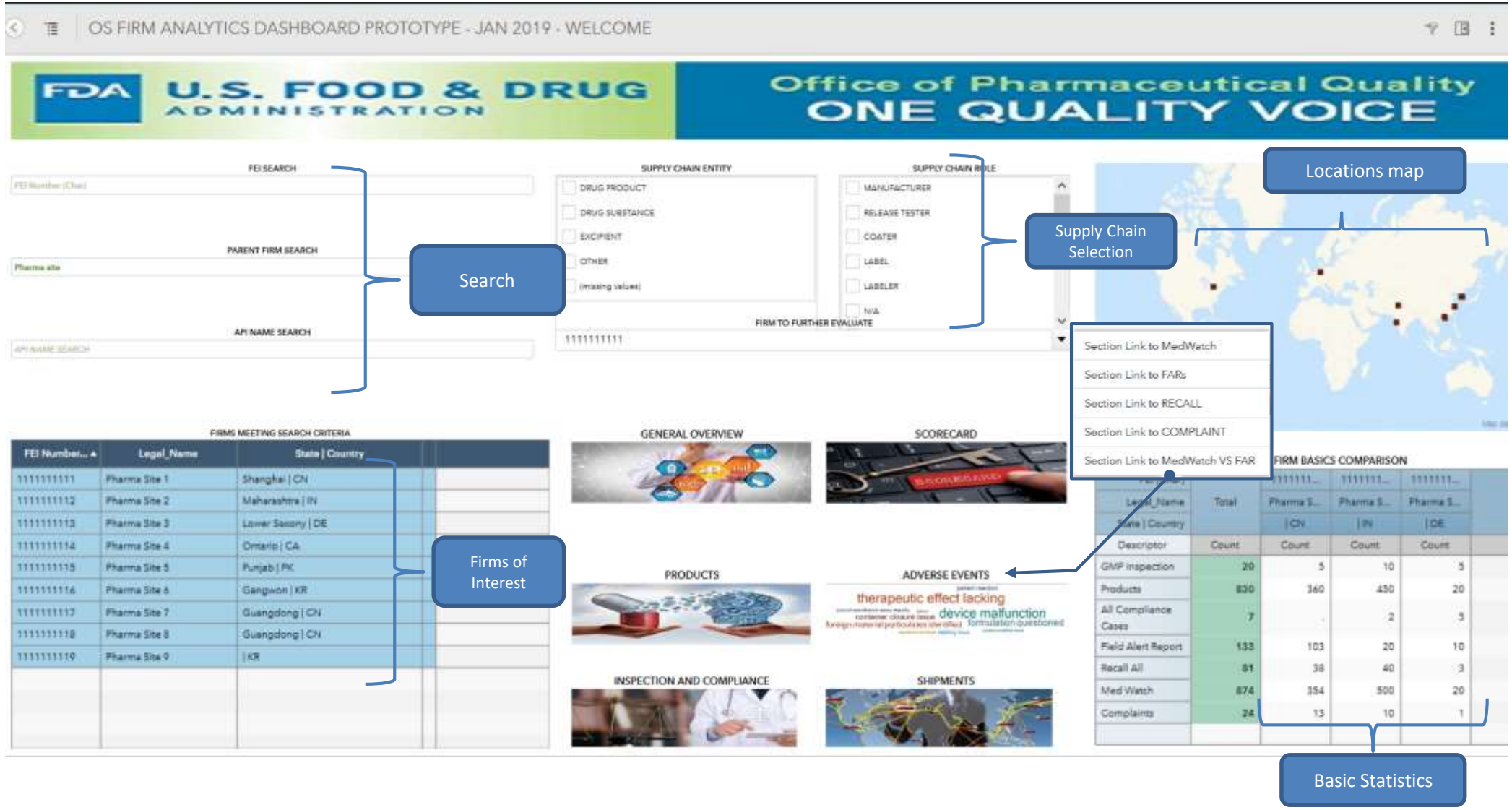
Report on the State of Pharmaceutical Quality

Available online https://www.fda.gov/media/125001/download

Key findings from FY 2018 Report:

- Inspection performance
  - Facilities which manufacture Application products have generally better inspection outcomes than sites which manufacture only over the counter (OTC) products.
  - Facilities which haven't had a surveillance inspection in over 10 years (or ever) are more likely to be out of compliance (31% Official Action Indicated (OAI) rate for first time inspections vs 15% OAI rate for sites previously inspected.
- Product Quality
  - Over a quarter of all recalls in FY 2013-2018 were attributed to manufacturers described as re-packers and re-labelers.
- Submission Quality
  - Applicants with the most submissions also had a higher rate of applications that are not approved.

Quality Surveillance Dashboard



New Inspection Protocols Project (NIPP)

Goals:

- **Modernize inspections through collecting structured data that can be analyzed so over time FDA can:**
  - Quantitate the state of pharmaceutical quality
  - Accelerate the pace of making informed, data-driven decisions
  - Lead to more efficient inspections in the future
  - Identify policy and outreach opportunities across the industry
  - Provide evidence for addition or modification of regulations

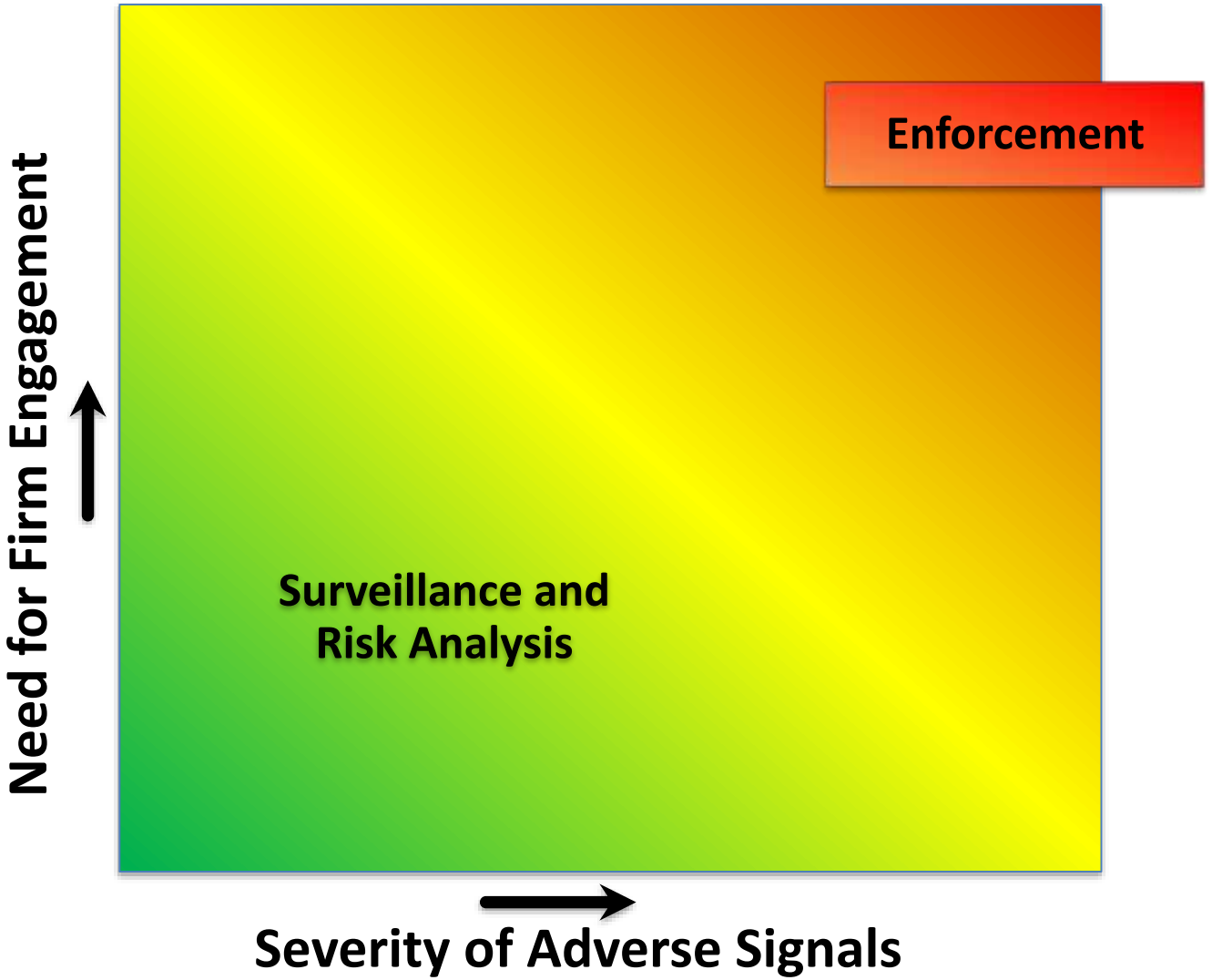
- **Identify attributes of an effective quality system and introduce these elements into the protocol**
  - Integration of quality culture elements (i.e. maturity indicators)

Site Engagement Program (SEP)

- Purpose:
  - Create an open line of communication between FDA and industry
  - Discuss both organizations' concerns to help mitigate or prevent CGMP production problems
  - Encourage collaboration
  - Integrate quality culture learnings into discussions
  - **This is a voluntary program**
- Benefits:
  - Collaborate on manufacturing issues that could impact drug product quality, availability, and ultimately patient care.
  - Lead to effective CAPAs that potentially reduce frequency or duration of surveillance inspection
- Initial Focus:
  - Sites whose quality issues are more likely to disrupt the availability of products vulnerable to shortage

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm622415.htm

Surveillance vs Enforcement



Take Aways

- OQS continually explores innovative ways to inform risk-based decisions for site and product quality and to assess quality management maturity:
  - New data sources
  - Predictive analytics to prioritize resources and identify potential quality problems
  - Machine learning techniques for proactive surveillance strategies
- Current research indicates quality metrics and quality culture programs are a good business practice and an important element of modern pharmaceutical manufacturing
- OQS continues to engage stakeholders and support related academic research
- **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**

Challenge Question

- Is this statement true or false?

  "If invited, facilities are required to participate in the Site Engagement Program"

- **FALSE**.

- This is a voluntary program.

Challenge Question

- FDA uses which of the following sources of information for quality surveillance?

  - Facility Data
  - MedWatch Reports
  - Sampling and Testing Results
  - A and C
  - All of the Above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