U.S. FOOD & DRUG ADMINISTRATION

Emerging Topics and Trends in Recent Inspections and How They Can Affect Application Approval

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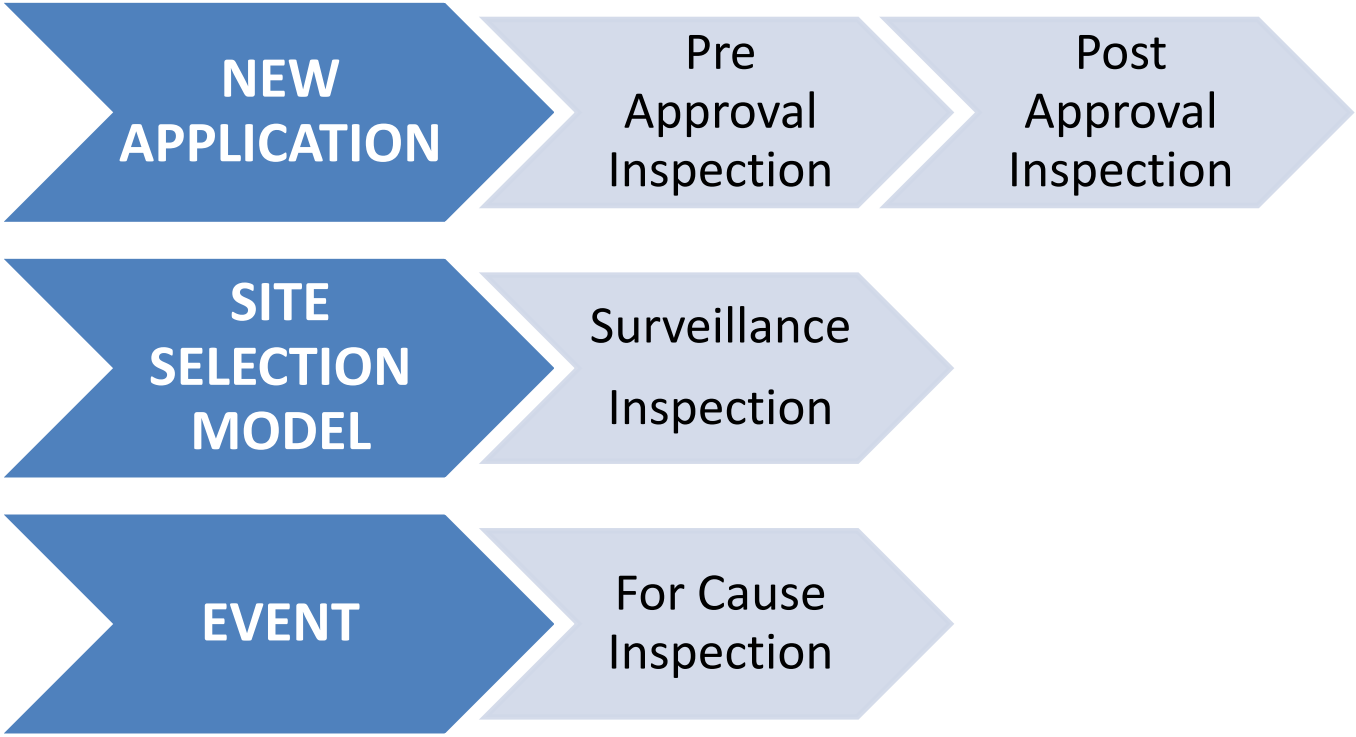
Objective

- High level overview the Drug Inspection Programs
- Overview of what Inspection data shows and emerging topics
- Overall recommendation on successful Inspections

Inspection Programs

There are few mechanisms that trigger an inspection as provided by The Food, Drug, and Cosmetic Act



Pre Approval Inspection Program

Designed to contribute to FDA's assurance that a manufacturing establishment named in a drug application is capable of manufacturing a drug, and that submitted data are accurate and complete

- Objective 1: Readiness for Commercial Manufacturing
- Objective 2: Conformance to Application
- Objective 3: Data Integrity Audit

CP 7346.832, "Pre-Approval Inspections/Investigations" Compliance Program Guidance Manuals (Human Drug GMPs)
https://www.fda.gov/media/71498/download

Surveillance Program

FDA

Scope includes ALL facilities manufacturing distributed products

Objectives:

- Determine compliance with CGMPS
- When necessary, provide evidence for enforcement actions to prevent adulterated product from entering the market
- Provide input to firms to improve compliance

Six systems:

- Quality
- Facilities and Equipment
- Materials
- Production
- Packaging and Labeling
- Laboratory Controls

Coverage:
of 2 or more systems, with *mandatory* coverage of the Quality System

Negative findings can result in enforcement actions

5

- E.g., warning letters, consent decree, import alert, etc.

Future of the Analytics Office Of Quality Surveillance

QUALITY SURVEILLANCE DASHBOARD

Provide a framework for consistent and up-to-date evaluation of facilities and potential quality signal within a product lifecycle

Incorporate interactive visualizations that enable users to discover and share insights regarding facilities Pharmaceutical Quality System (PQS) effectiveness, manufacturing capabilities and potential product quality issues

Utilize predictive analytics and natural language processing to enable efficient and risk-based assessments

Integrate and govern facility and post market product quality data from across multiple systems both internal and external to the agency

Text Analytics Methods used to evaluate Surveillance Inspection Observations

- Not every observation is mapped to 21 CFR in our system

  (for example, API manufacturer inspection citations OR some Form 483 are in pdf format only)

- CFR level citations may have more tha

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed. specifically, batch investigation records were not completed per the firm's policy xxxx "batch investigation record…….range. all of the batches included below were reviewed and approved by the quality unit for release without the completion of a batch investigation ……

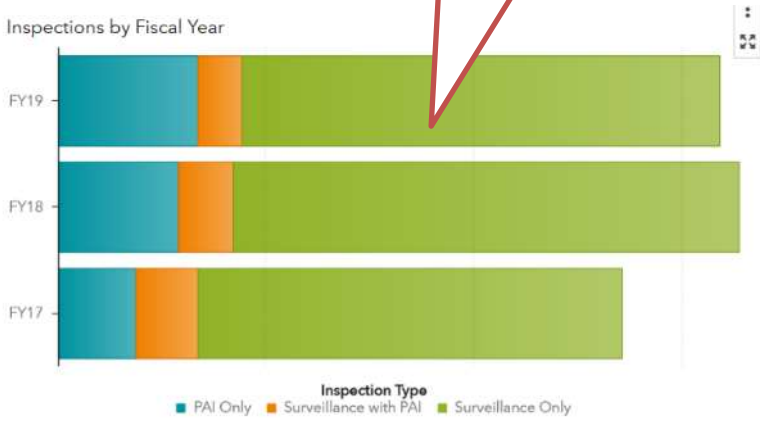
Pattern Matching
211.192 : There is a failure to thoroughly review [any unexplained discrepancy] [the failure of a batch or any of its components to meet any of its specifications] ---. Specifically, ***

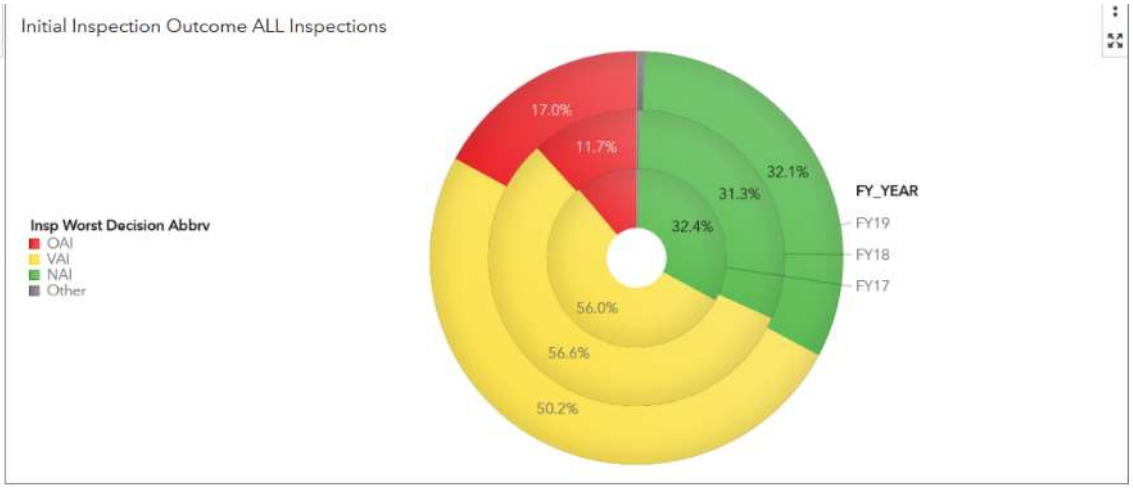
Natural Language processing
TOPIC 1 - Investigation

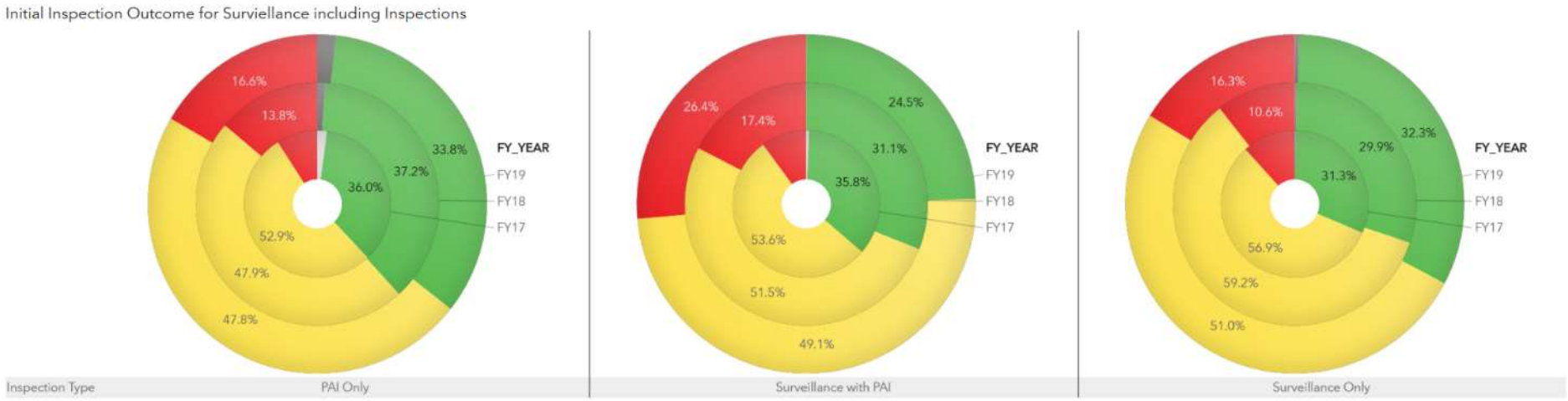
Natural Language processing
TOPIC 2 – Quality Responsibility

Over 75% of Inspections are Surveillance

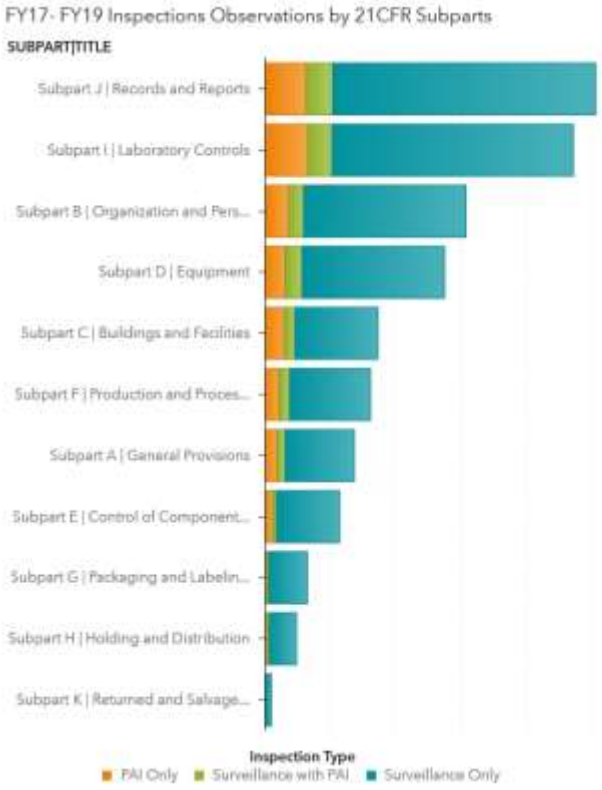
FY17 – FY19 INITIAL OUTCOMES FOR SURVEILLANCE INSPECTION

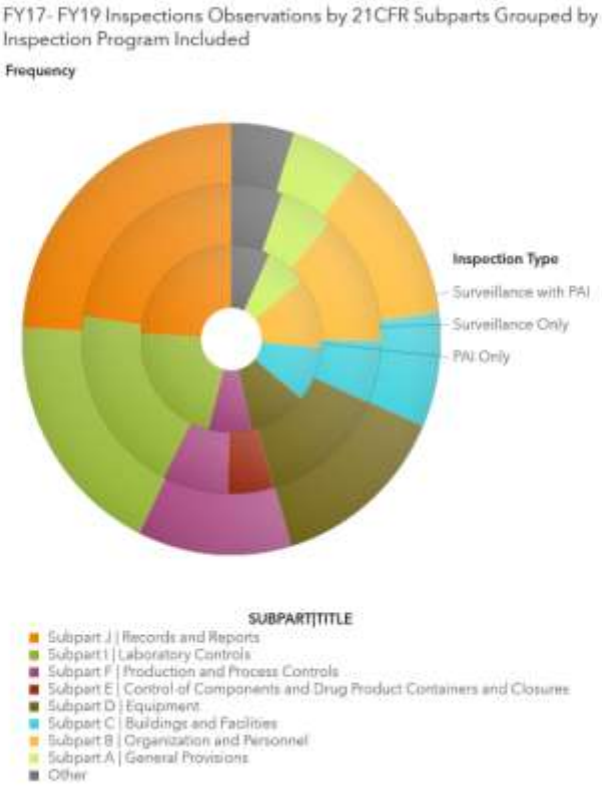


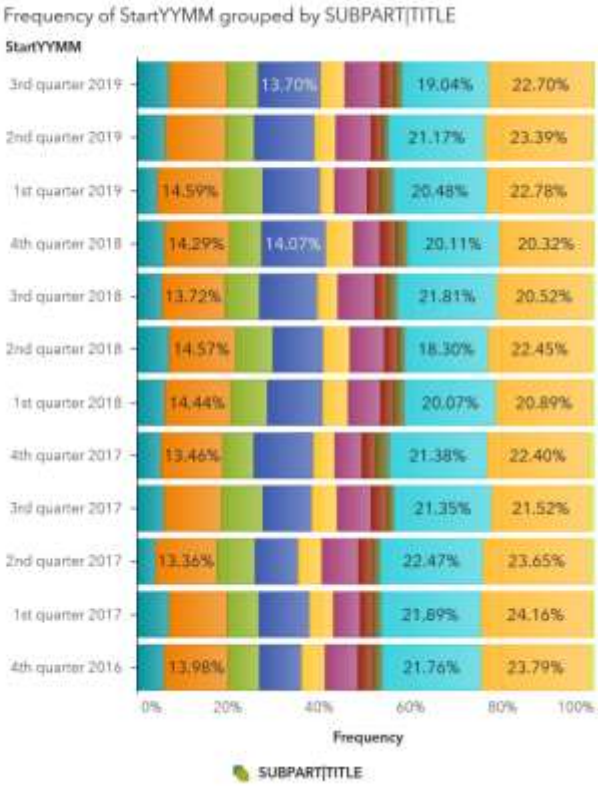




OVERVIEW OF INSPECTION





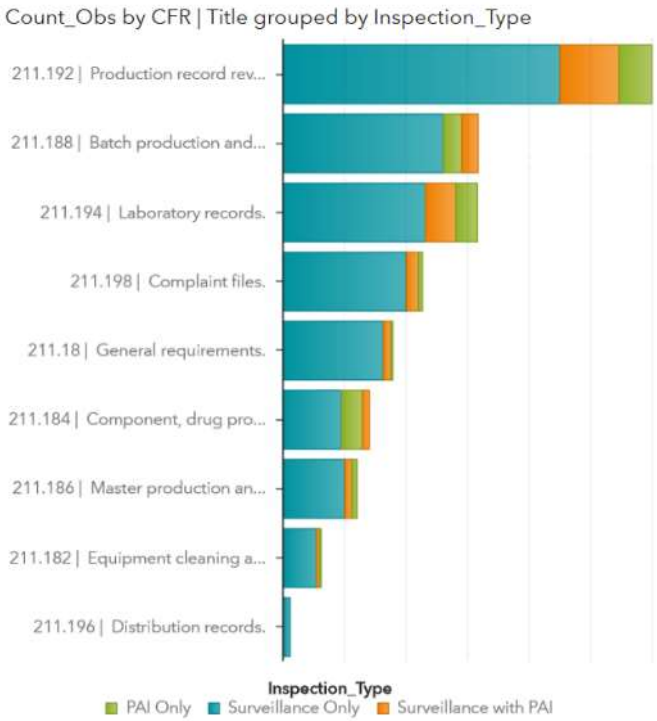


Emerging Topics – Records and Reports

Emerging Topics FY17 - FY19 from 21CFR Observations

SubPart Title

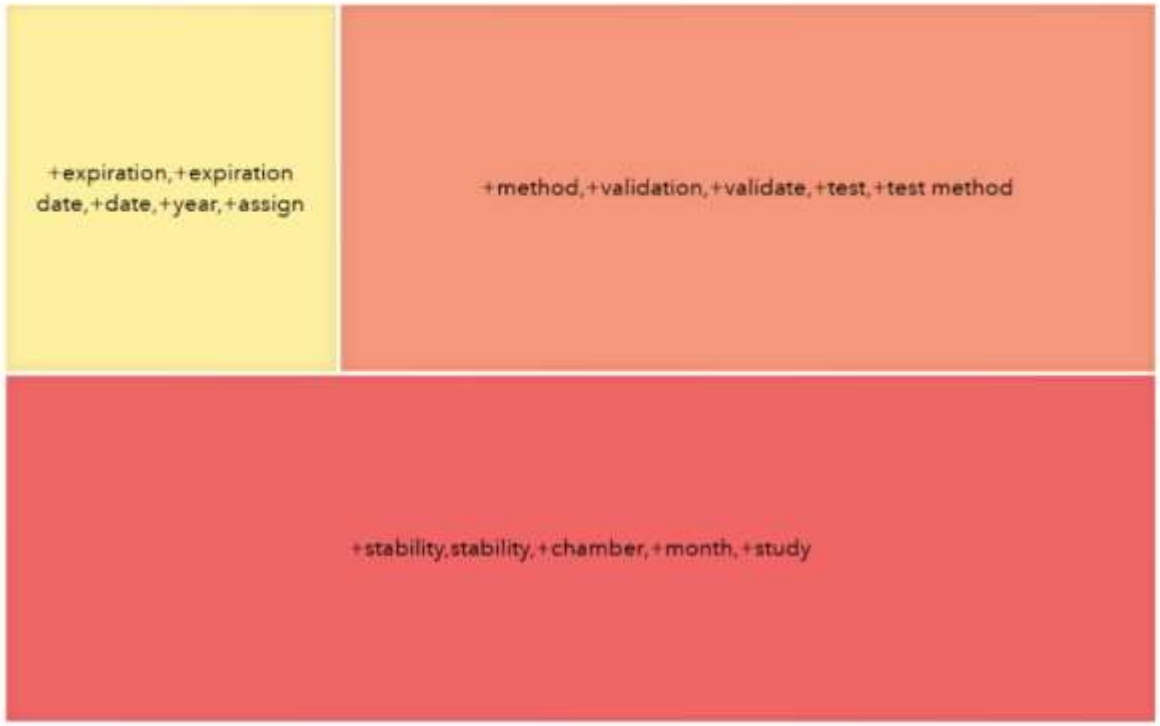
Records and Reports

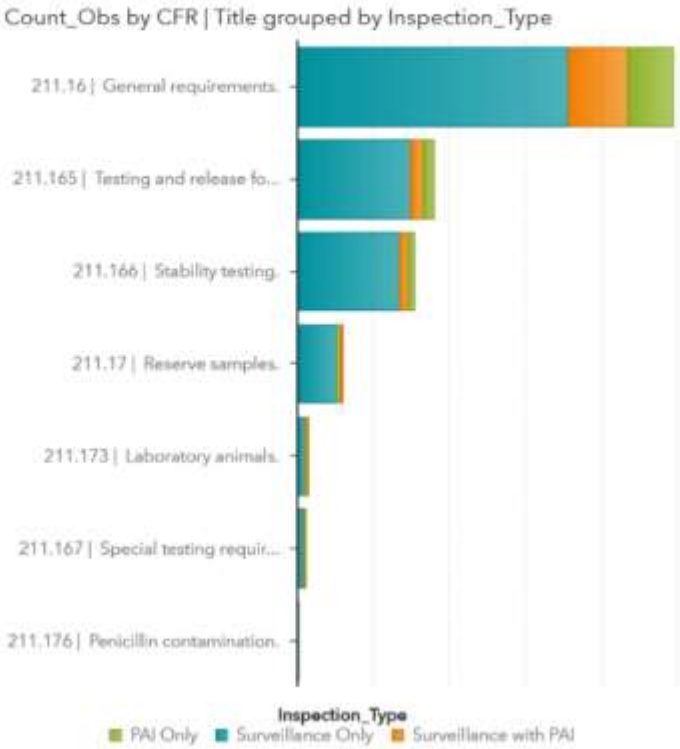


Emerging Topics – Laboratory Controls

Emerging Topics FY17 - FY19 from 21CFR Observations

SubPart Title
Laboratory Controls

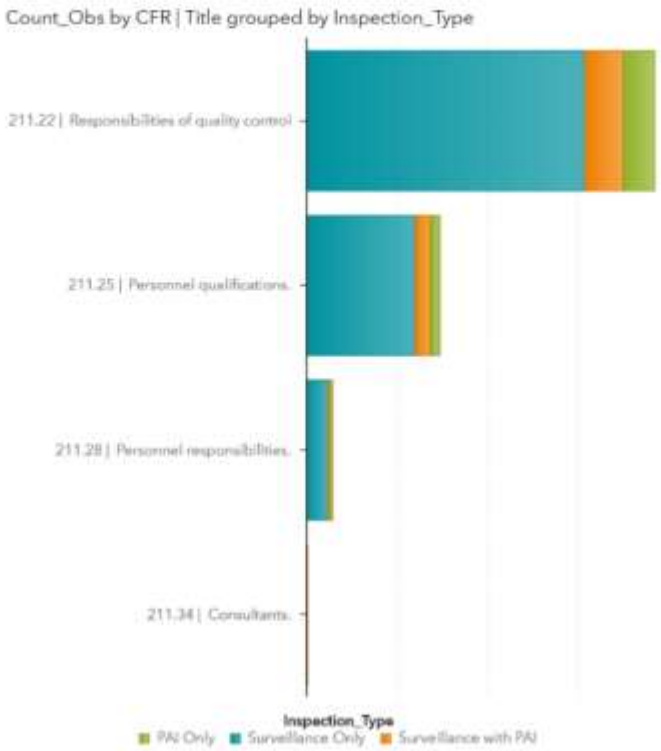




Emerging Topics – Operation and Personnel

Emerging Topics FY17 - FY19 from 21CFR Observations

Organization and Personnel



Tips Towards Successful Inspection

- Have a **robust** commitment to quality that includes an enhanced quality management system that focuses on **continual improvement**
- Strive for **mature quality management** across the organization that demonstrates product quality and its impact on the patient drives corporate strategy and decision.
- Be aware of significant issues before inspection; **CAPAs** executed and effectiveness is quantified
- Senior management is aware of potential issues – ensure programs exist for escalating quality issues
- Consider previous inspection findings: address specific issue, and implement **global** corrections
- Ensure robust **supplier qualification and management programs** are in place

Challenge Question

How many systems are in the CDER Surveillance inspection program

A. 4
B. 7
C. 6
D. 2

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