FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS

Knock, Knock, FDA is Here; Be Prepared for a Regulatory Inspection

Joanne Schlossin, Consumer Safety Officer
Karen Kosar, BIMO Specialist
BIMO-East

President Ronald Reagan (4/12/86)

"The nine most terrifying words in the English language are: 'I'm from the government and I'm here to help.'"

That was then…

- We want to ensure you have access to tools and resources to help you and your staff succeed.
- FDA Centers and Field Offices are available to speak with you.
- Small Business Reps
- Ombudsman

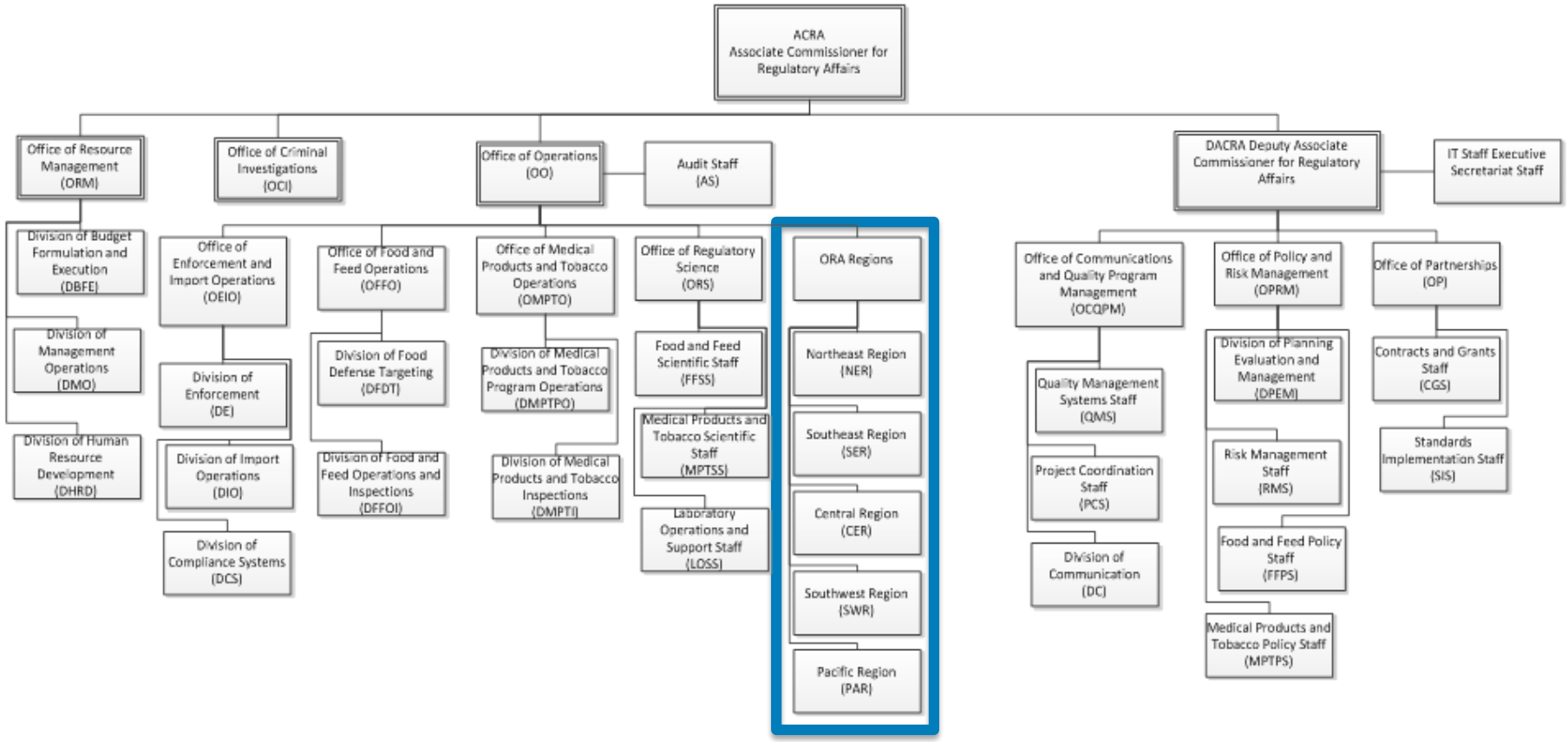
FDA Inspections

- [A Quick] Intro to FDA Post Program Alignment
- Before FDA arrives
- While FDA is on-site
- As the inspection closes
- Common observations
- Following the inspection

Intro to FDA Post Program Alignment

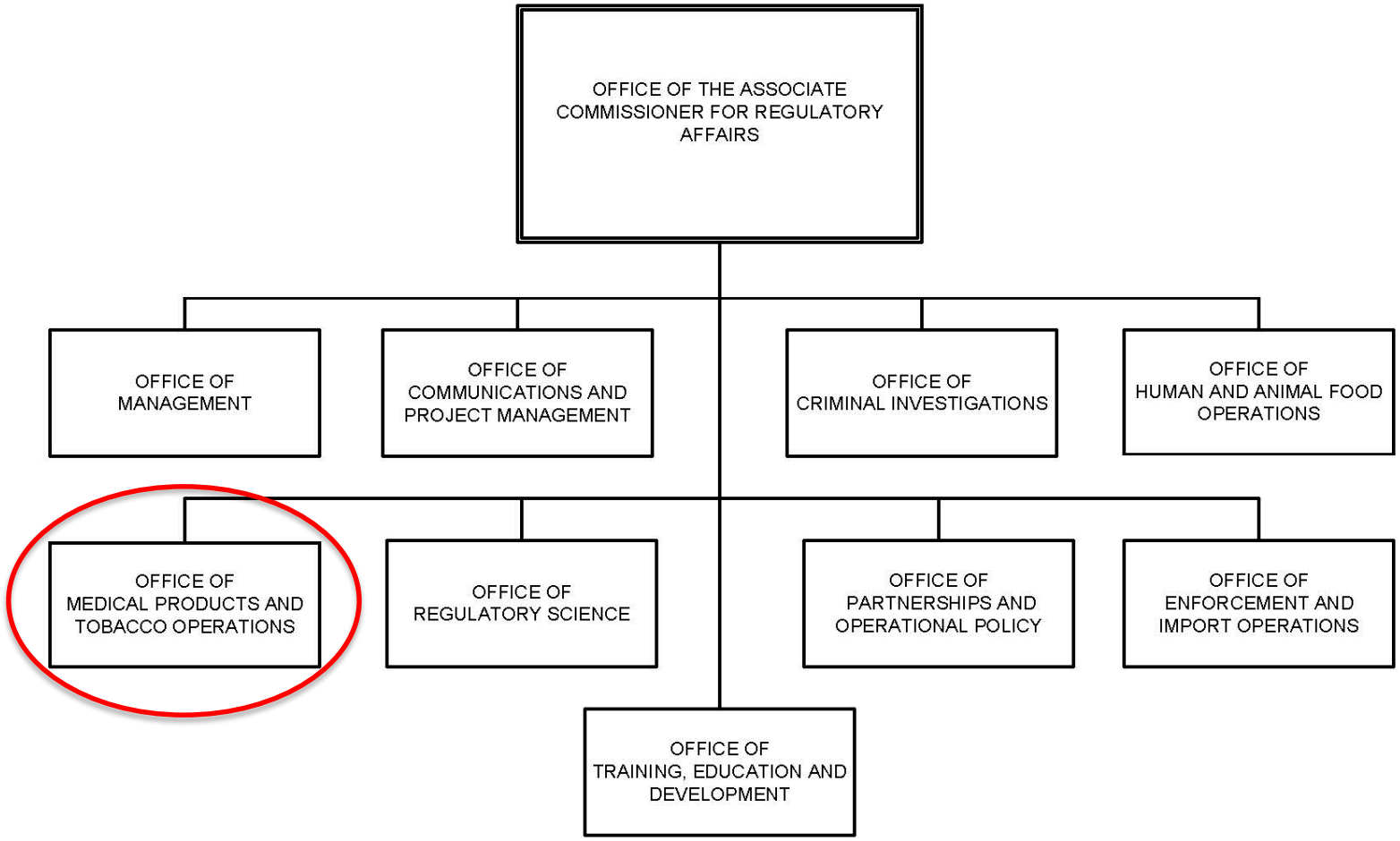
OLD

Geographically Aligned Organizational Model



New

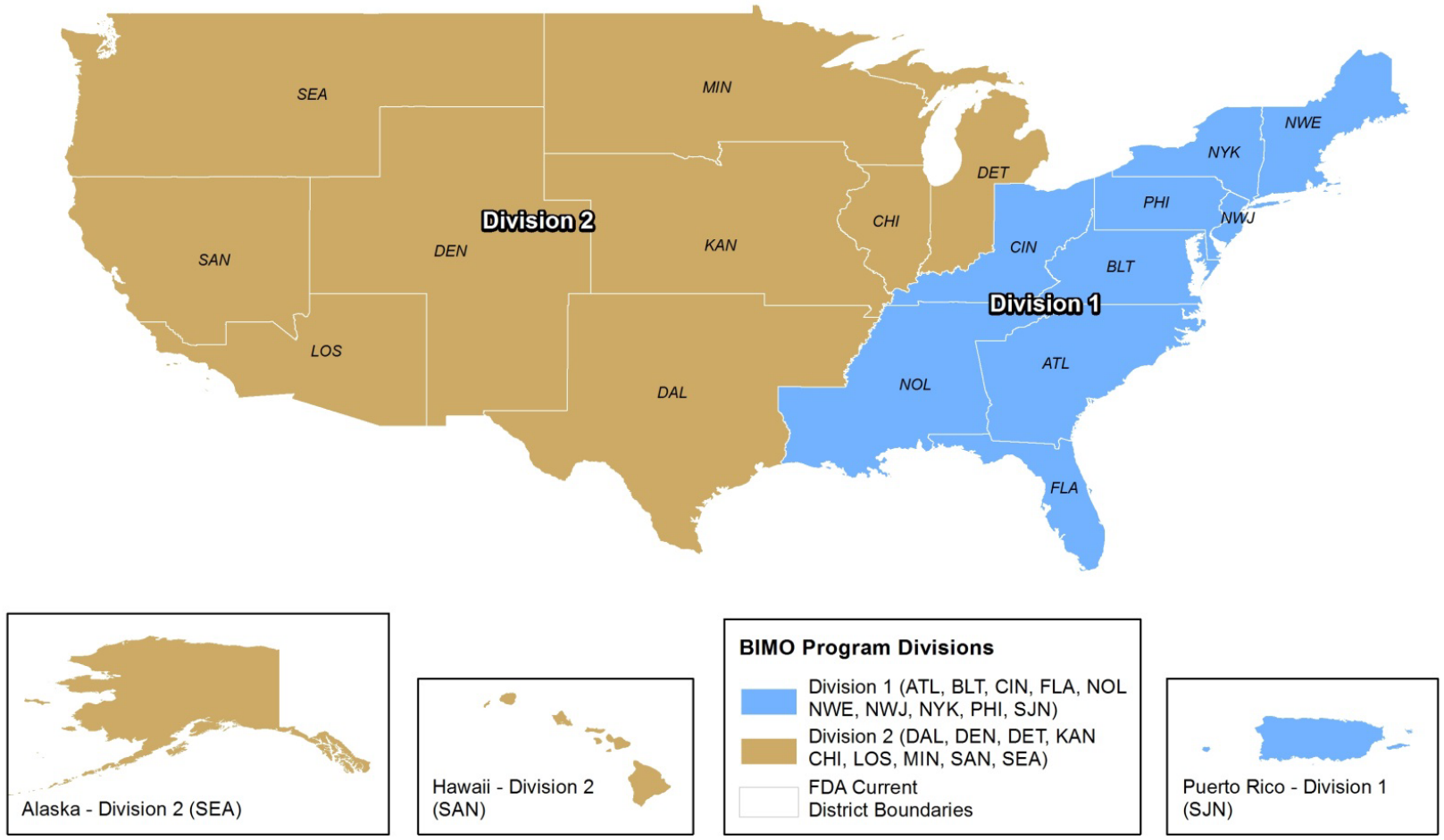
Program Aligned Organizational Model



Program Alignment: Key Changes

From	To
Geographic management of operations	Program management of operations, management teams based on staff: • Bioresearch Monitoring 2 management teams • Biologics 2 management teams • Human and Animal Food 12 management teams • Medical Device and Radiological Health 3 management teams • Pharmaceutical Quality 4 management teams • Tobacco • Plus Imports as a program 5 management teams
SES Regional Food & Drug Directors	SES Program Directors
Degrees of program specialization for investigations, compliance and operational managers	Exclusive specialization in one program for investigations, compliance and operational managers
20 District Directors who manage the geographic district and all programs operations within the district	20 District Directors who manage the geographic district and only one program for operations. Plus eight new program division directors who manage program operations only – total 28 management teams
One import district and a range of import operations embedded within the 16 other districts	Five import divisions (four new import divisions) covering all borders, managing import operations nationally as a program

Office of Bioresearch Monitoring Operations



Office of Bioresearch Monitoring Operations

Chrissy Cochran, PhD
Director
Office of Bioresearch Monitoring Operations

David Glasgow
Deputy Director

Anne Johnson
DD PHI-DO/ PDD Div I

Eric Pittman
PDD Div II

Amy Ray
Special Assistant

Christine Smith
DIB Div I

Audrey Vigil
DIB Div II

Have you been involved in an FDA Inspection?

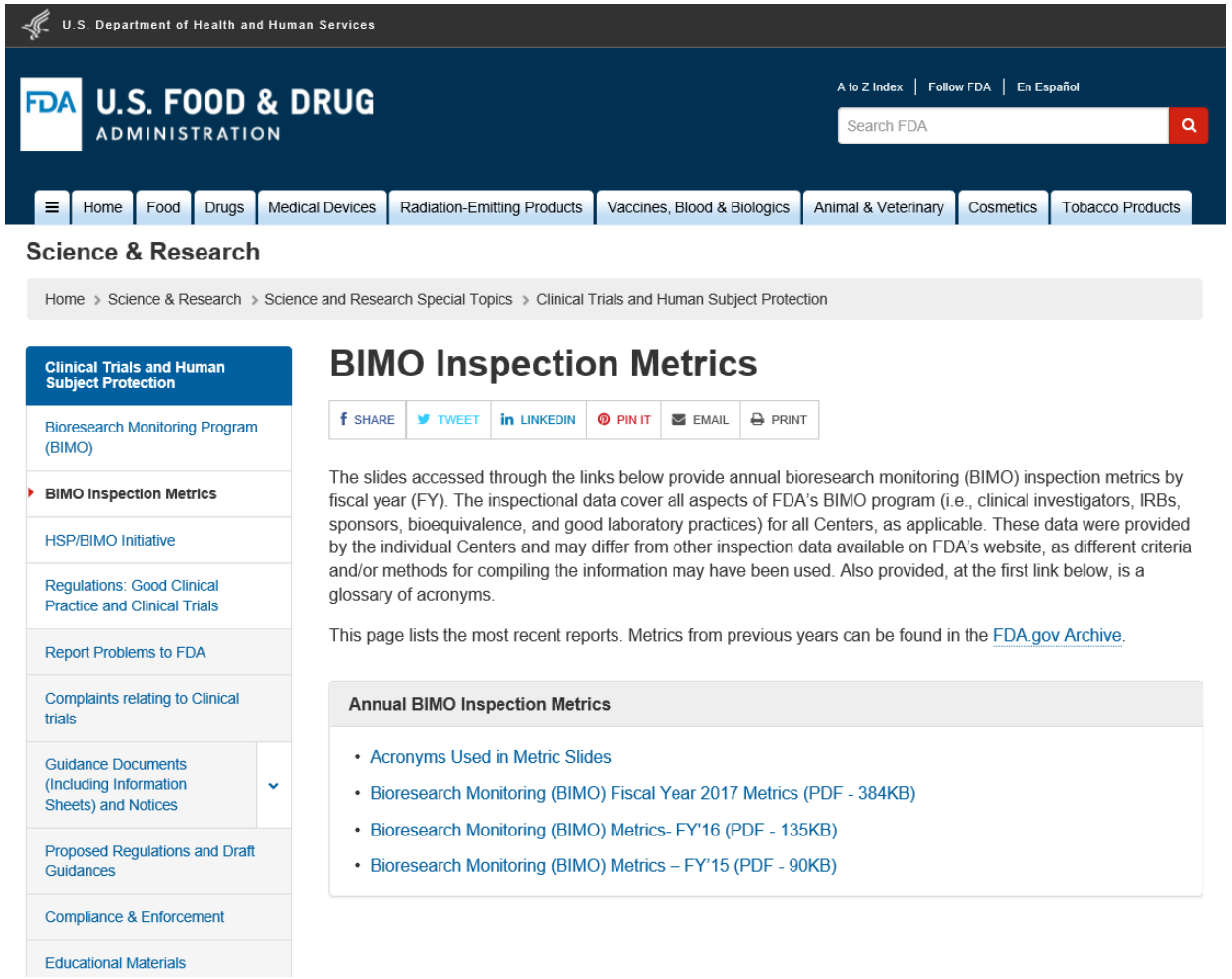
How prepared were you?

Before FDA Arrives…

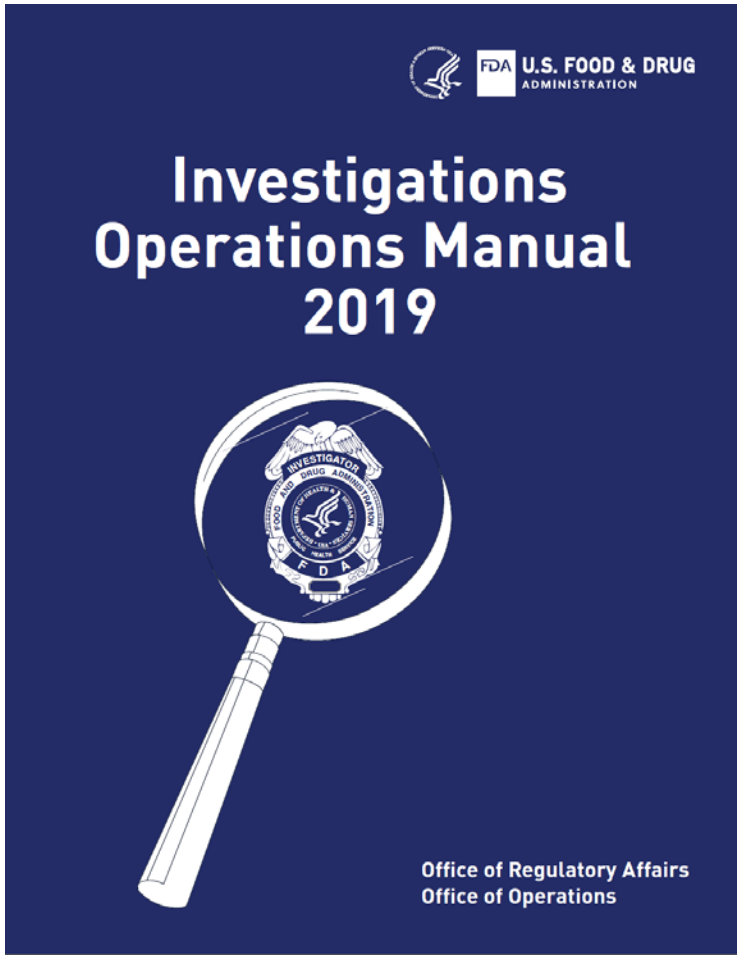
- Be in compliance!
  - Have the appropriate staff
  - Provide training to staff on regulatory requirements, specific protocol requirements, any processes or procedures
  - Facilitate open communications
  - Not just the what, but the why compliance matters
  - Assume all studies conducted will be inspected
- Be prepared for an inspection
  - Have procedures for how to handle an inspection
  - Mock inspection with staff; use sponsor audits as a tool
  - When an investigator calls, know to whom to route them

Before FDA Arrives…

- Know FDA BIMO Metrics!
  - Visit https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm261409.htm
    - Top observations
  - Read posted warning letters



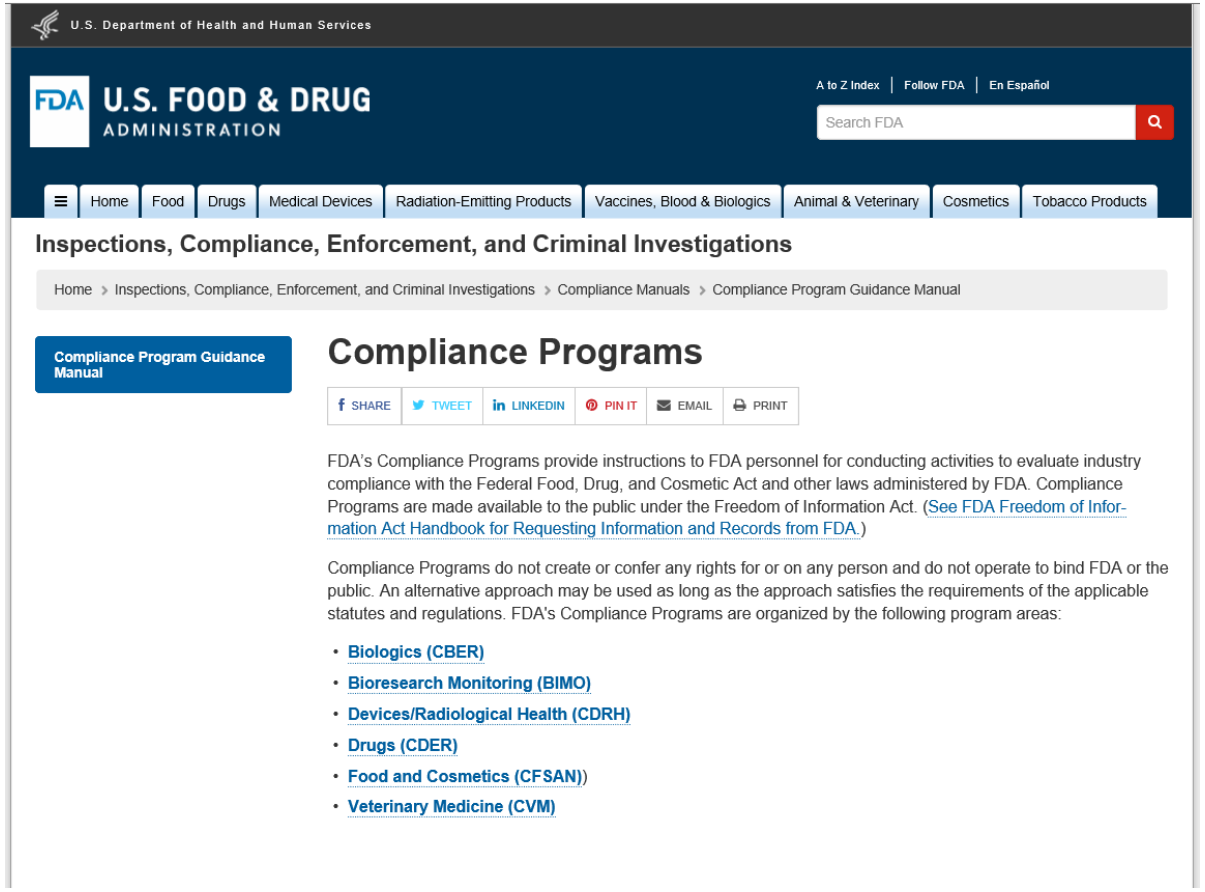
Know what we know…



- Investigations Operations Manual

  -Visit: https://www.fda.gov/ICECI/Inspections/IOM/default.htm
- This is the ORA Field Procedural Manual. What we do, is in here.
- If nothing else, you should be familiar with Chapter 5 (and Chapter 4 for BEQ)

Know what we know…



- Compliance Program Guidance Manual
  - Compilation of Compliance Programs that supplement our IOM and provide specific procedures and internal guidance to our field and center staff.
  - Visit: https://www.fda.gov/ICECI/ComplianceManuals/ComplianceProgramManual/default.htm

Know what we know…

Compliance Programs are split into different sections:

I-Background (Law, regs, etc)

II-Implementation

III-Inspectional

IV-Analytical

V-Regulatory/Administrative

VI-References/Program Contacts

VII- HQ Responsibility

PROGRAM 7348.811
CHAPTER 48- BIORESEARCH MONITORING
CLINICAL INVESTIGATORS AND SPONSOR-INVESTIGATORS
Date of Issuance: December 8, 2008
Guidance for FDA Staff

SUBJECT:
Clinical Investigators and Sponsor Investigators

IMPLEMENTATION DATE
December 8, 2008

REVISION:

COMPLETION DATE
Continuing

DATA REPORTING	
PRODUCT CODES	PROGRAM ASSIGNMENT CODES
FACTS does not require product codes for Bioresearch Monitoring Inspections	09811 Food Additives
	41811 Biologics (Cell; Gene Transfer)
	42811 Biologics (Blood)
	45811 Biologics (Vaccines)
	48811 Human Drugs
	68811 Animal Drugs
	83811 Medical Devices

FIELD REPORTING REQUIREMENTS:

For domestic inspections, copies of all establishment inspection reports (EIRs), complete with attachments, exhibits, and any related correspondence are to be submitted promptly to the Center contact, who is generally the reviewer in the Center's Bioresearch Monitoring (BIMO) program identified in the assignment.

While FDA is on-site

- Opening meeting
  - FDA-482; credentials
  - Scope of inspection
  - Schedule
  - Explain roles and responsibilities, study conduct
  - Explain records, organization, access
- Objective is to ensure investigator and site staff have clear communication and expectations

While FDA is on-site

- During the inspection
  - Be accessible to answer questions, provide copies
  - Don’t delay unnecessarily, if time is needed to retrieve records/answer, explain why
- Daily wrap up
  - Questions?
  - Concerns?
  - Progress?
  - Plan for following day?

As the inspection closes

- Schedule close out meeting, ensure responsible/knowledgeable parties available
- Is there an FDA-483?
  - Observations clear?
  - Do you have additional documentation not reviewed during inspection?
  - Verbal response? Will be included in Establishment Inspection Report
  - Plan to respond in writing?

After the Inspection has ended

- If there was an FDA-483 – should respond in writing
  - Recap observation
  - Provide explanation if appropriate
  - Describe corrective actions considered and when they will be implemented including any SOP revisions, staff training
  - Consider impact on any other on-going or future studies
- No FDA-483, but discussion items?
  - Consider any impacts and corrective actions you may need to do
  - Consider a written response, the items will be reported in the Establishment Inspection Report and reviewed

Written Responses

- Will be reviewed by investigator and center
- Will be considered if any regulatory/administrative action is contemplated
- Thorough responses help!
- If you respond, please do so within 15 days!

METRICS*

* HTTPS://WWW.FDA.GOV/SCIENCERESEARCH/SPECIALTOPICS/RUNNINGCLINICALTRIALS/UCM261409.HTM

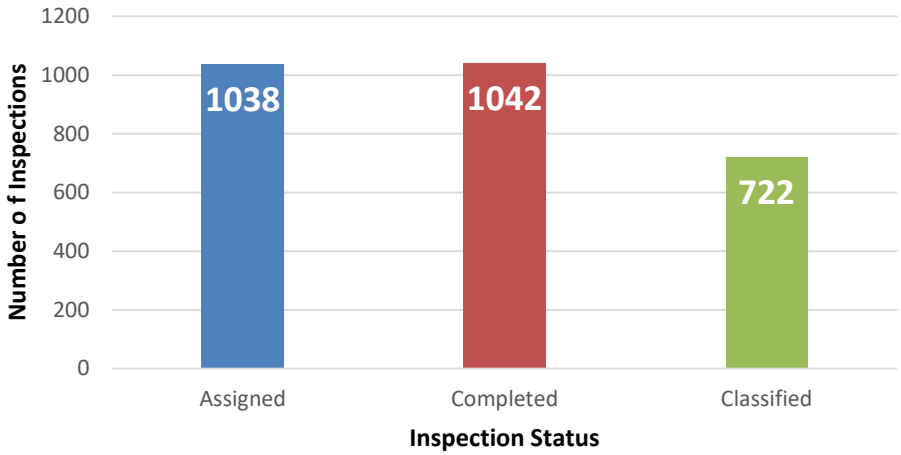
ENFORCEMENT ACTIONS
FY'19

Untitled Letters – 1

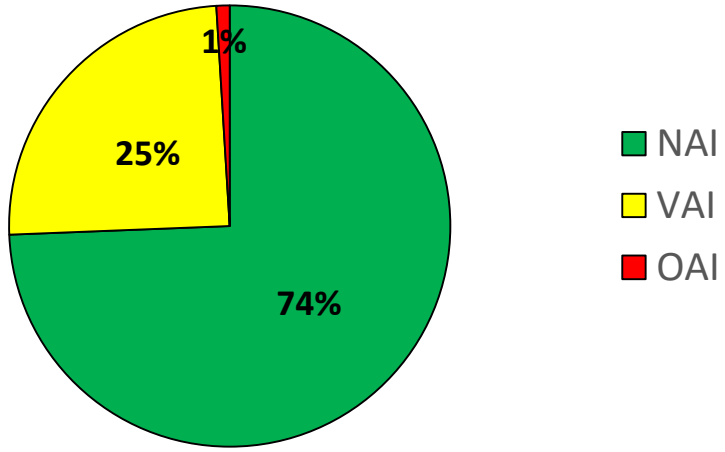
Warning Letters –5

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN (NIDPOE) – 0 (most recent March 2018)

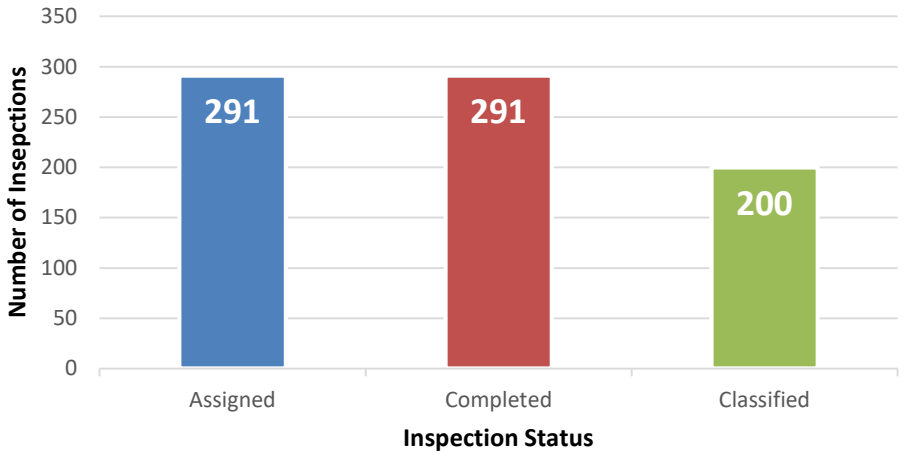
FY18 Domestic Inspections



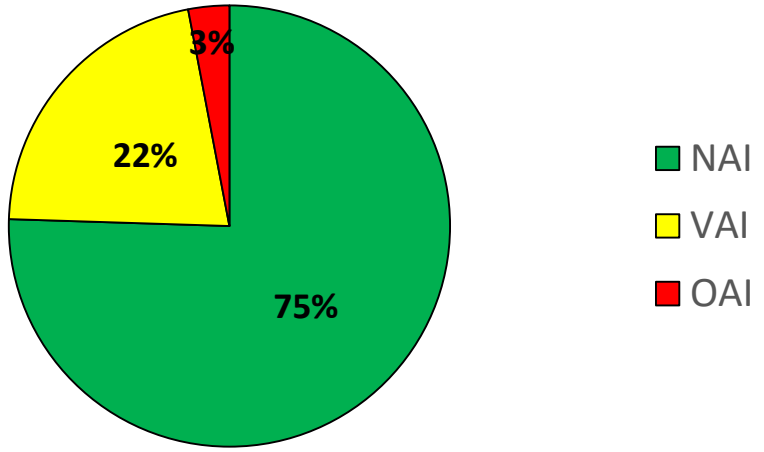
FY18 Domestic Inspections Classified



FY18 Foreign Inspections



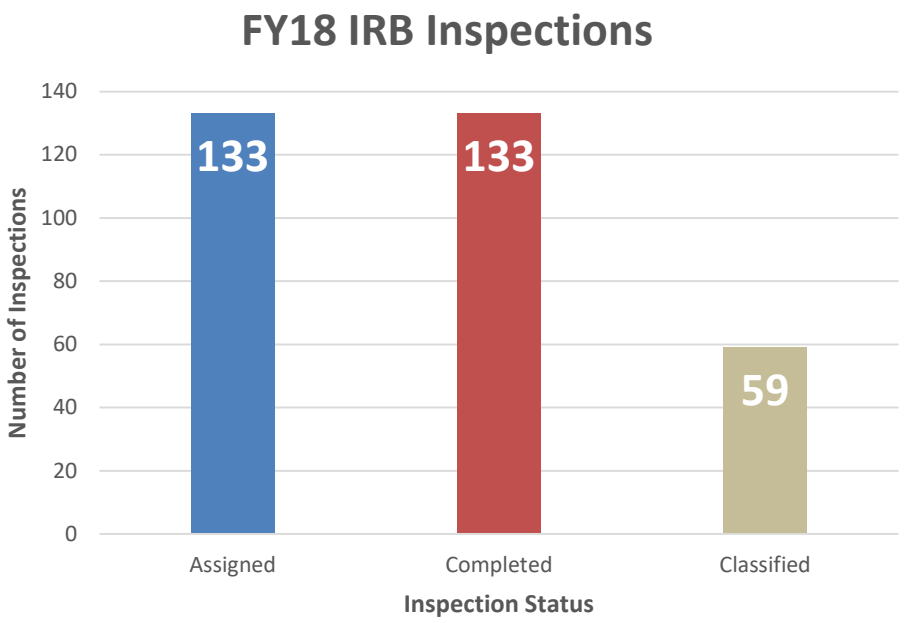
FY18 Foreign Inspections Classified

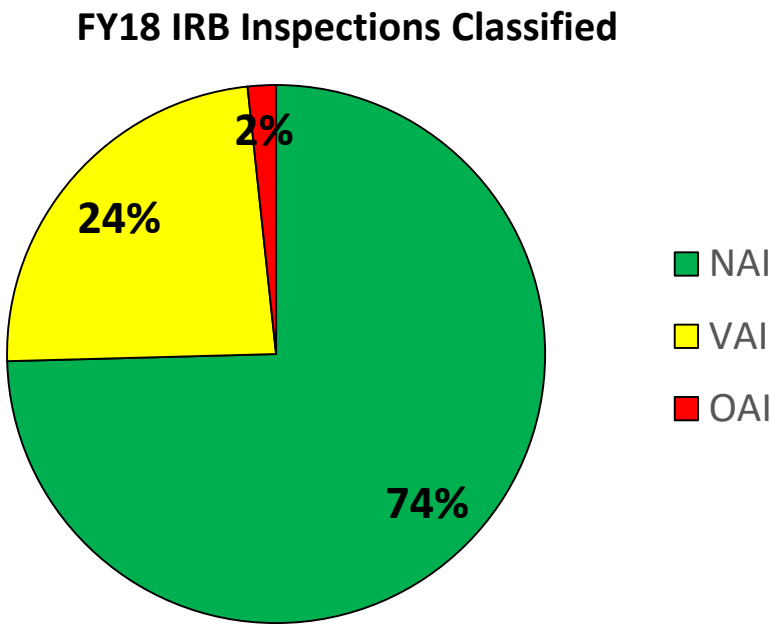


Common International* Deficiencies

- Similar to domestic inspectional findings
- Sponsor inspections
  - Inadequate monitoring
  - Failure to bring investigators into compliance
- CI inspections
  - Protocol deviations
  - Inadequate investigational product accountability
  - Inadequate subject protections

*Deficiencies identified in FDA Form 483 issued at close of inspections.

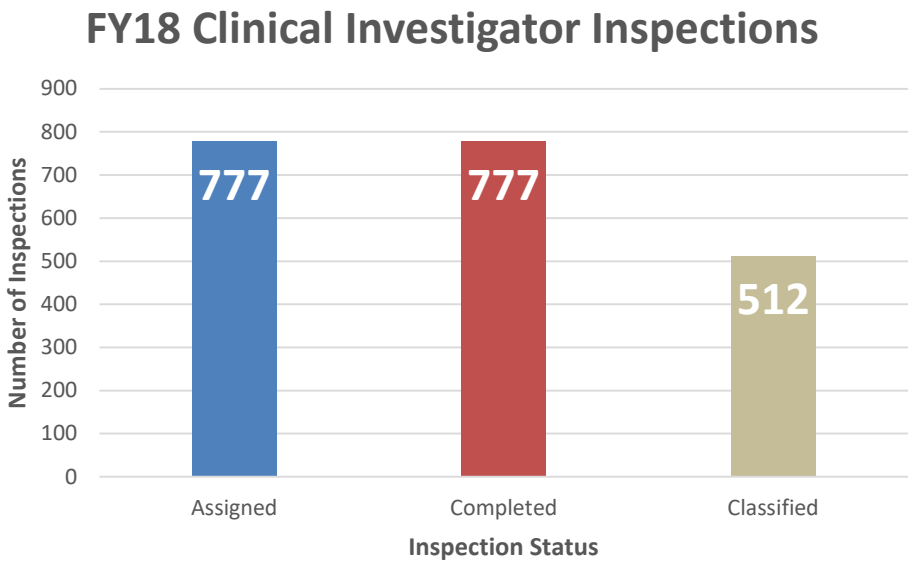

FY18 IRB Inspections
140
120
100
80
60
40
20
0
Number of Inspections
133
133
59
Assigned
Completed
Classified
Inspection Status

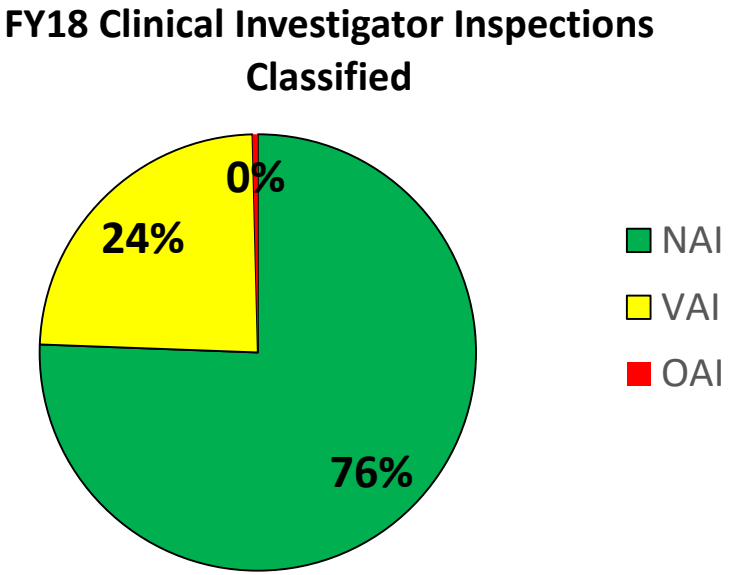

FY18 IRB Inspections Classified
2%
24%
74%
NAI
VAI
OAI

Common IRB Deficiencies*

- Inadequate initial and/or continuing review
- Inadequate written procedures
- Inadequate meeting minutes, membership rosters
- Quorum issues
- Prompt reporting of non-compliance, suspension or termination
- Subpart D issues
- Lack of or incorrect SR/NSR determination

*Institutional Review Board (CP 7348.809) deficiencies identified in FDA Form 483 issued at close of inspections.

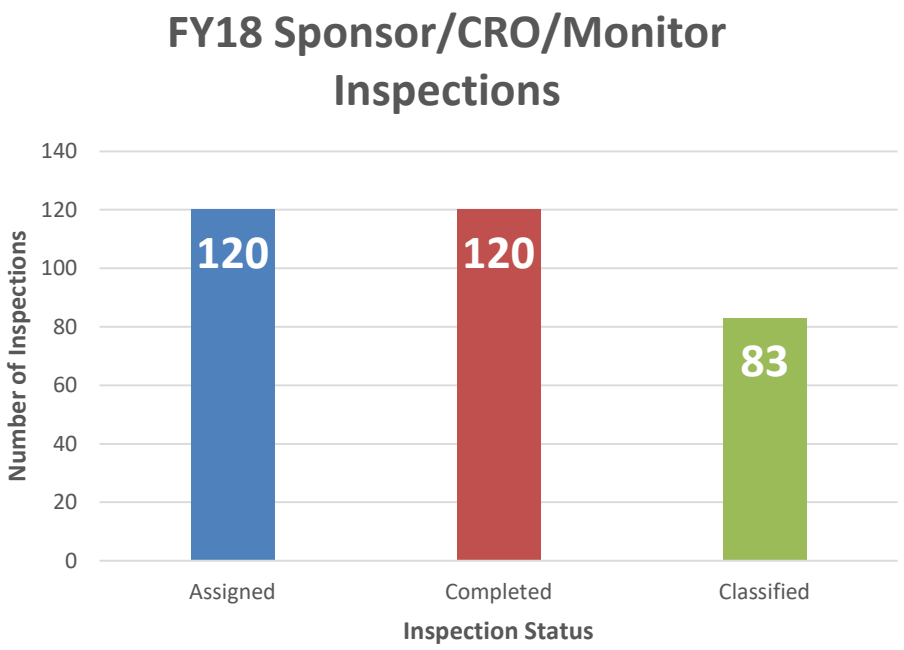

FY18 Clinical Investigator Inspections
900
800
700
600
500
400
300
200
100
0
Number of Inspections
777
777
512
Assigned
Completed
Classified
Inspection Status

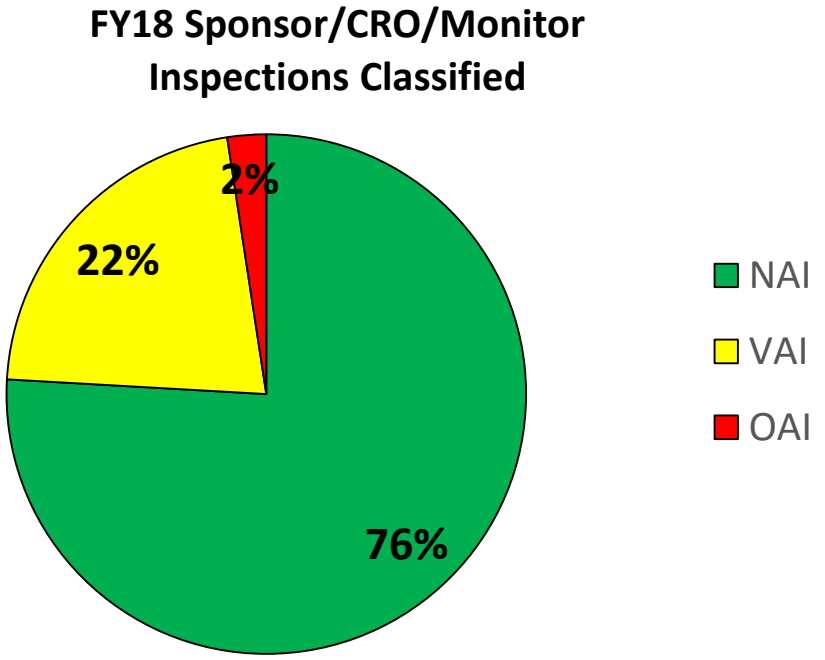

FY18 Clinical Investigator Inspections Classified
0%
24%
76%
NAI
VAI
OAI

Common Clinical Investigator Deficiencies*

- Failure to follow the investigational plan/agreement or regulations, or both
- Protocol deviations
- Inadequate recordkeeping
- Inadequate subject protection – informed consent issues, failure to report AEs
- Inadequate accountability for the investigational product
- Inadequate communication with the IRB
- Investigational product represented as safe/effective

* Clinical Investigator (CP 7348.811) deficiencies identified in FDA Form 483 issued at close of inspections.

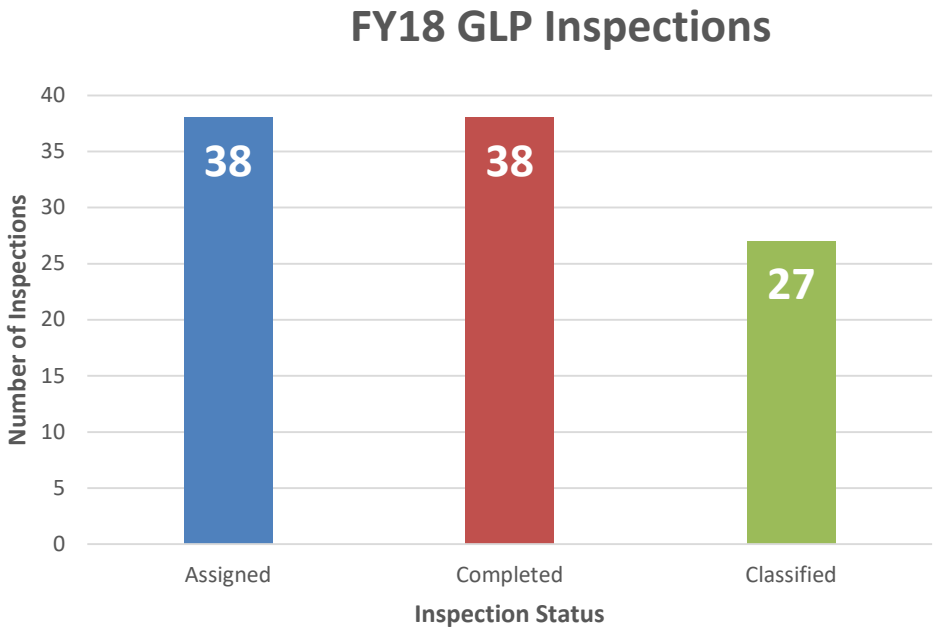

FY18 Sponsor/CRO/Monitor Inspections
140
120
100
80
60
40
20
0
Number of Inspections
120
120
83
Assigned
Completed
Classified
Inspection Status

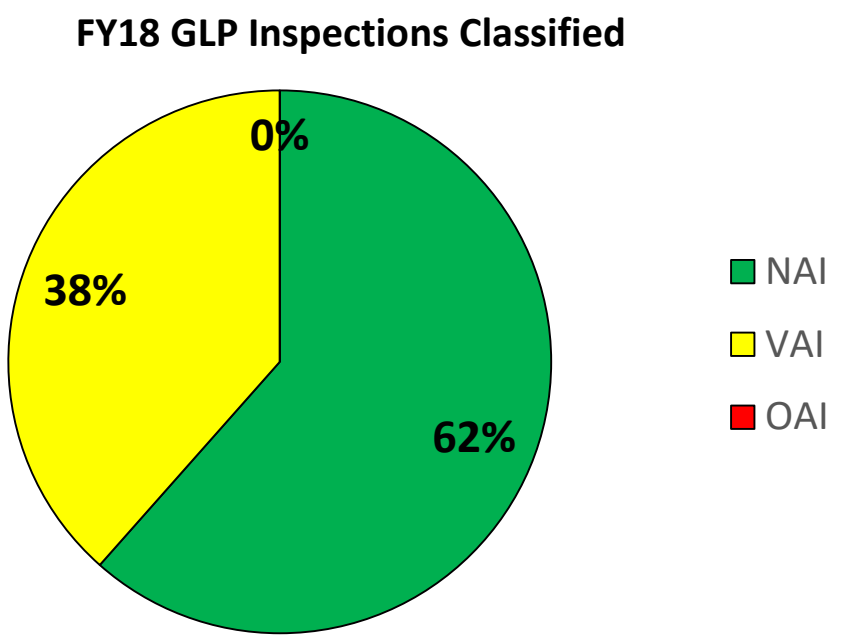

FY18 Sponsor/CRO/Monitor Inspections Classified
2%
22%
76%
NAI
VAI
OAI

Common S/M/CRO Deficiencies*

- Inadequate monitoring
- Failure to bring investigators into compliance
- Inadequate accountability for the investigational product
- Failure to obtain FDA and/or IRB approval prior to study initiation

*Sponsors, Contract Research Organizations, and Monitors (CP 7348.810) deficiencies identified in FDA Form 483 issued at close of inspections.


FY18 GLP Inspections
40
35
30
25
20
15
10
5
0
Number of Inspections
38
38
27
Assigned
Completed
Classified
Inspection Status


FY18 GLP Inspections Classified
0%
38%
62%
NAI
VAI
OAI

So…

Violations Can Be Avoided

- As I mentioned previously, ensuring staff understand the protocol and regulatory requirements will aid in conducting research in compliance with the regulations
- Training
  - Make it effective for your staff
  - Most sites provide training and yet there are still violations
  - Not just standard GCP training, but training tailored to the study requirements

Investigator Interaction

- Most investigators are well trained professionals…
- Each site and study are different, help the investigator understand how your site works and any specific study requirements that may be unique
- What to do when there are disagreements between investigator and study staff
- Should I fear retaliation?

Contacts to know

- FDA-482 will list the geographical district office and phone number
- Program Director, Deputy Program Director, Program Division Director, Director, Investigations
- Ombudsman

- **Program Director**
  - Chrissy Cochran – Chrissy Cochran@fda.hhs.gov (301) 796-5663

- **Deputy Program Director**
  - David Glasgow – David.Glasgow@fda.hhs.gov (301) 796-5403

- **BIMO East Director**
  - Anne Johnson – Anne.Johnson@fda.hhs.gov (215) 717-3003

- **BIMO West Director**
  - Eric Pittman – Eric.Pittman@fda.hhs.gov (312) 596-4259

ORA Ombudsman

Currently Vacant

- The ORA Ombudsman is dedicated to two primary objectives:
  - Informally address concerns, complaints, and other issues that arise between ORA and stakeholders outside of the Agency, including industry, governmental organizations (federal, state, territorial, and tribal), and other members of the public; and
  - Engage in outreach and education for these stakeholders and employees of ORA to enhance communication and transparency with stakeholders.

ORAOmbudsman@fda.hhs.gov
240-535-6021

QUESTIONS

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