Preparing for a United States Food and Drug Administration (FDA) Inspection: VOICE

This project has been funded in whole or in part with Federal funds from the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract No. N01-AI-50022, entitled HIV Clinical Research Support (CRS) Services.

Agenda

8:00a – 8:10a	**Introduction and Course Objectives**
8:10a – 9:00a	**Section I**
	- Overview of US FDA and the Inspection Process
	- Inspection Preparation and Readiness
	- Using FDA Resources
9:00a – 9:10a	**Break**
9:10a – 10:20a	**Section II**
	- OCSO Trend Analyses Overview
	- Quality Management (QM) and the Clinical Quality Management Plan (CQMP)
	- Roles and Responsibilities
	- Key Quality Indicators
10:20a – 10:30a	**Break**
10:30a – 11:50a	**- QM Implementation and Documentation**
	- Problems and Trends Found – Now What?
11:50a – 12:00p	**Conclusion**

Objectives

At the conclusion of this presentation, VOICE site staff will be able to:

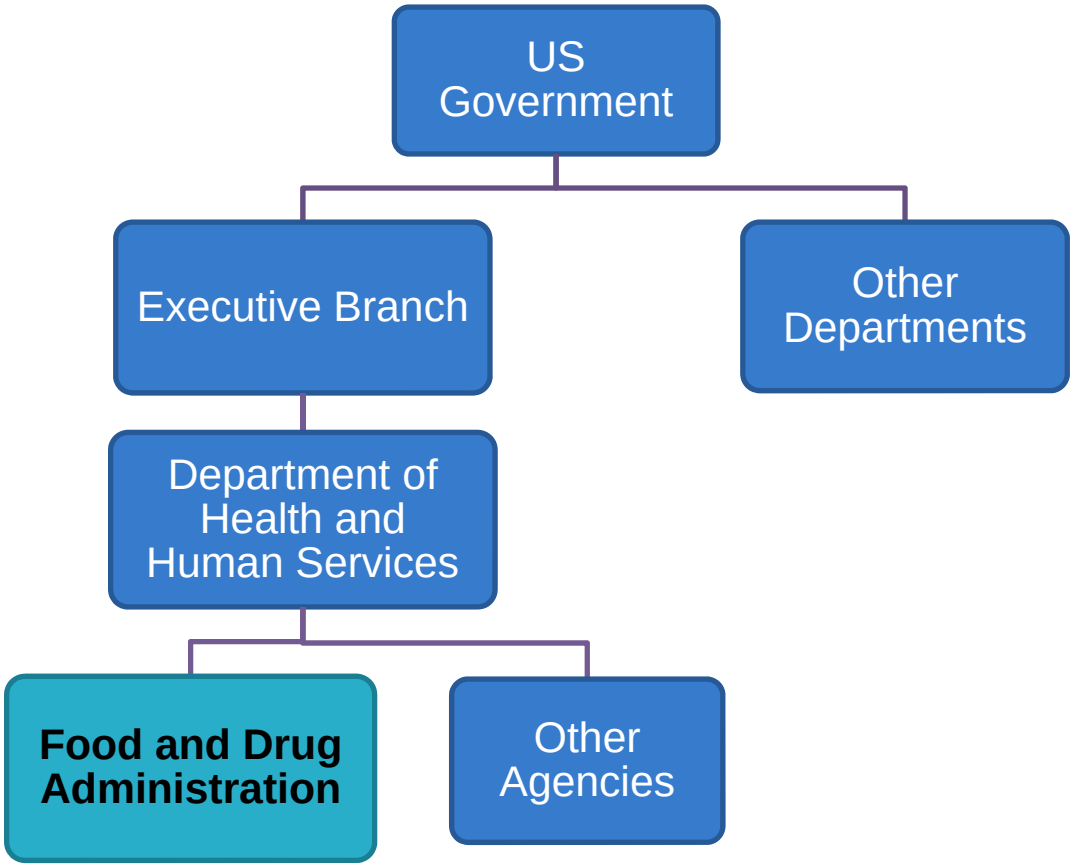
- Explain the FDA inspection process
- Identify FDA inspection documents and outline the purpose and flow of each
- Identify areas for improvement from the site-specific trend analysis that may require attention prior to an FDA inspection
- Identify resources available to the site and how to use them in preparation for an FDA inspection

Objectives Continued

- Describe the relationship between quality management activities and FDA inspection preparedness
- Implement quality management techniques that will assist with identification of areas for improvement in preparation for a possible FDA inspection

Overview of the United States Food and Drug Administration (FDA) and FDA Inspection Process

FDA



The FDA is an agency within the Department of Health and Human Services (DHHS) of the US Government.

FDA's Mission

Protecting Public Health

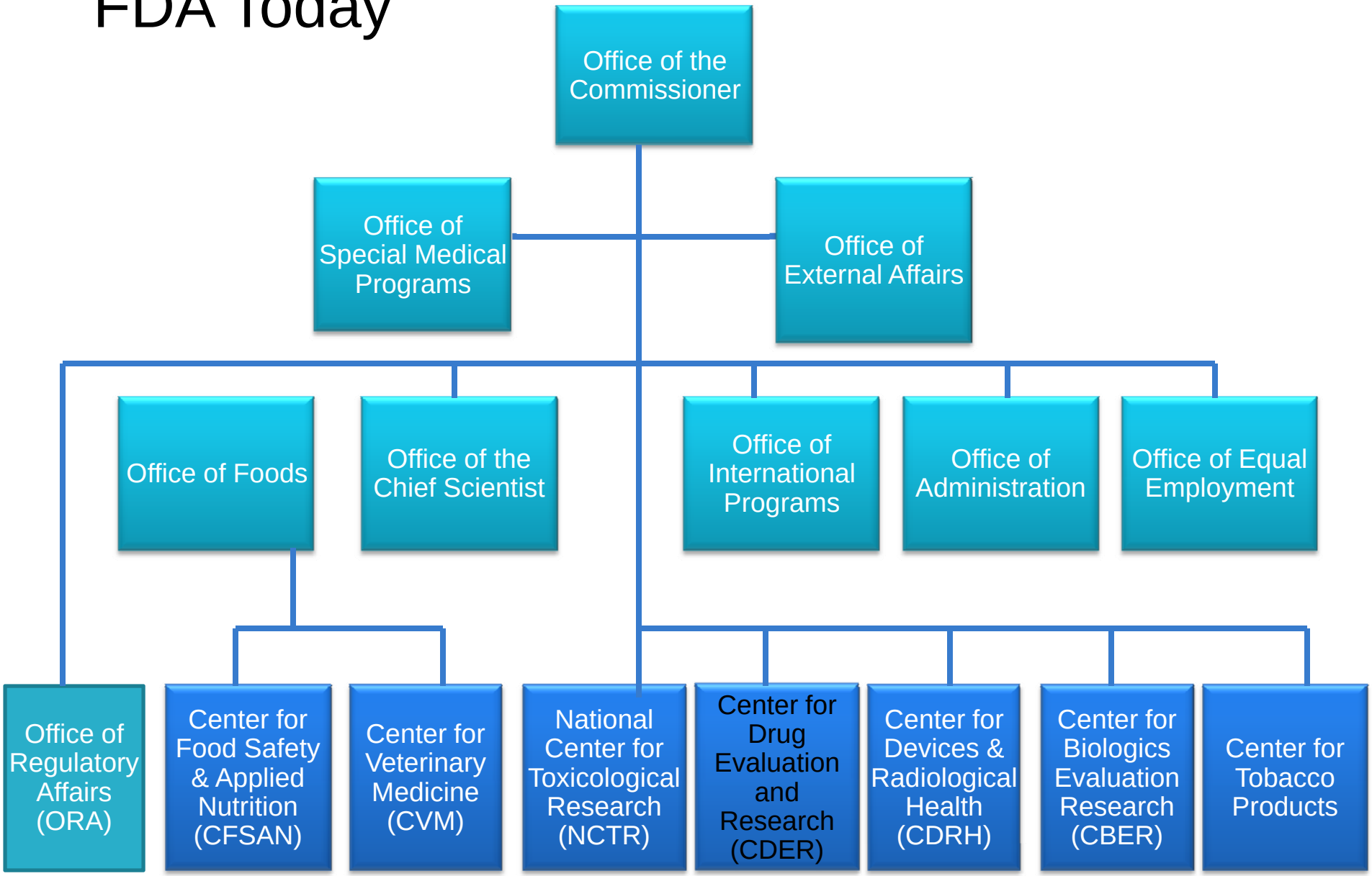
- Assuring **safety, efficacy, and security of human drugs, biological products, and medical devices,** as well as veterinary drugs, cosmetics, products that emit radiation, and the US food supply.

Advancing Public Health

- Helping to **speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines** and foods **to maintain and improve their health**.
- Regulating the manufacturing, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by minors.

http://www.fda.gov/AboutFDA/CentersOffices/default.htm

FDA Today


Office of the Commissioner
Office of Special Medical Programs
Office of External Affairs
Office of Foods
Office of the Chief Scientist
Office of International Programs
Office of Administration
Office of Equal Employment
Office of Regulatory Affairs (ORA)
Center for Food Safety & Applied Nutrition (CFSAN)
Center for Veterinary Medicine (CVM)
National Center for Toxicological Research (NCTR)
Center for Drug Evaluation and Research (CDER)
Center for Devices & Radiological Health (CDRH)
Center for Biologics Evaluation Research (CBER)
Center for Tobacco Products

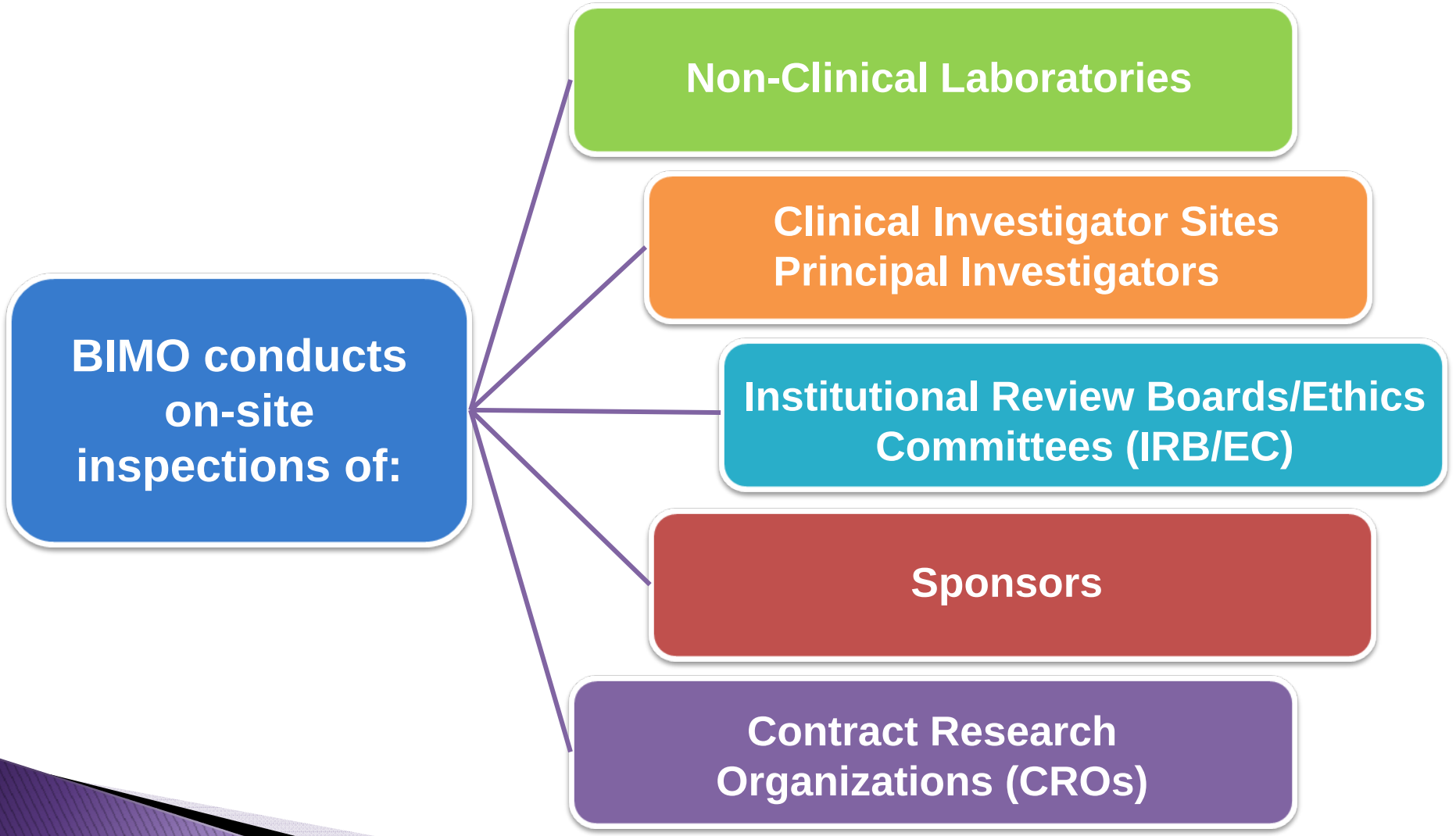
Bioresearch Monitoring (BIMO) Overview

Bioresearch Monitoring (BIMO) Program

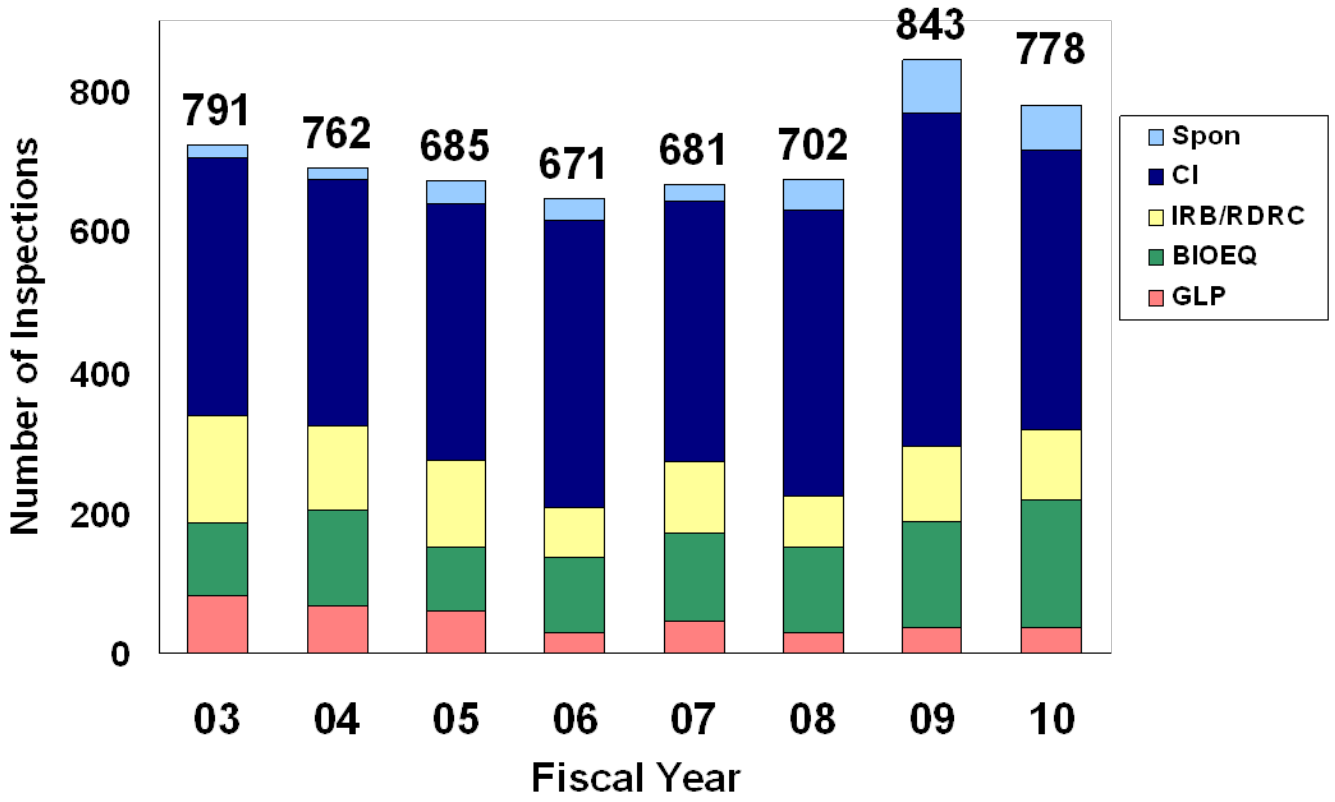
- An FDA program designed to monitor all aspects of the conduct and reporting of FDA-regulated research by conducting on-site inspections and data audits
- Inspections are conducted domestically and internationally
- Over 1000 inspections are conducted annually
- Routine and directed inspections

http://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/ucm133562.htm

Bioresearch Monitoring (BIMO) Program



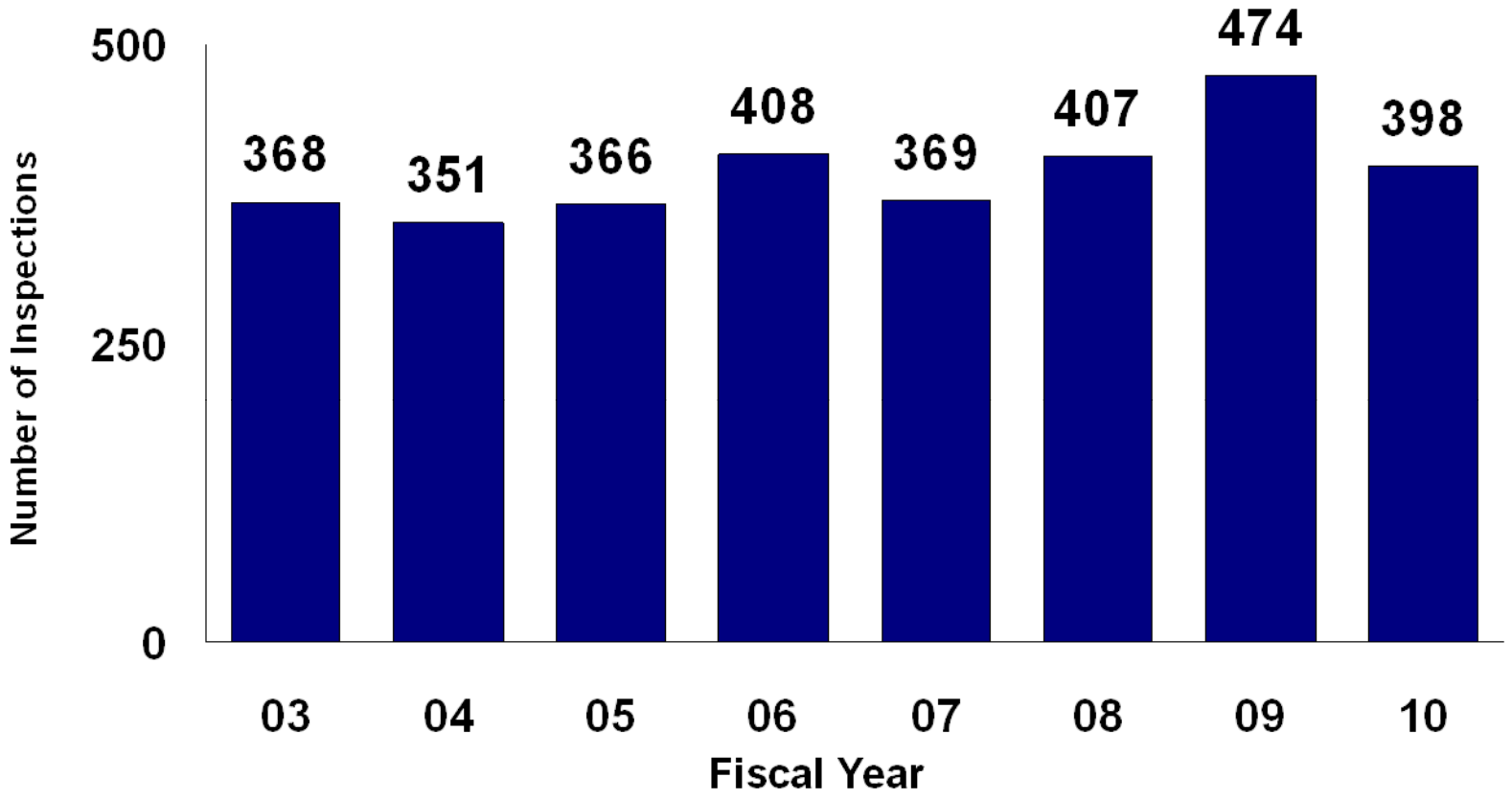
Bioresearch Monitoring Program Inspections* (CDER, FY 2003-2010)



*Based on inspection start date – DSI database [4/01/2011]
IRB/RDRC include some CBER/CDRH related Inspections

http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM256376.pdf

Clinical Investigator Inspections (CDER, FY 2003-2010)



http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM256376.pdf

Routine vs. Directed Inspections

Routine Inspection

- Large volume of work
- Efficacy too good
- Toxicity too low
- Out-of-range laboratory results
- Pivotal study
- Submitted for new drug application
- Site has singular importance

Directed Inspection

- Past FDA inspection history
- Whistleblower reports
- Complaints
- FDA/Sponsor raised issues
- High protocol noncompliance
- Large volume of clinical trials
- Work outside of specialty
- Inconsistent safety reporting
- Unusually high enrollment
- High number of subjects with disease

Purpose of Inspections

- Ensure protection of human subjects
- Verify data
  - Quality and integrity
- Verify compliance with regulations and GCP guidance
- Verify control of study product
- Facilitate sound decision making
  - Safety and efficacy

Regulations

Title 21 Code of Federal Regulations (CFR)

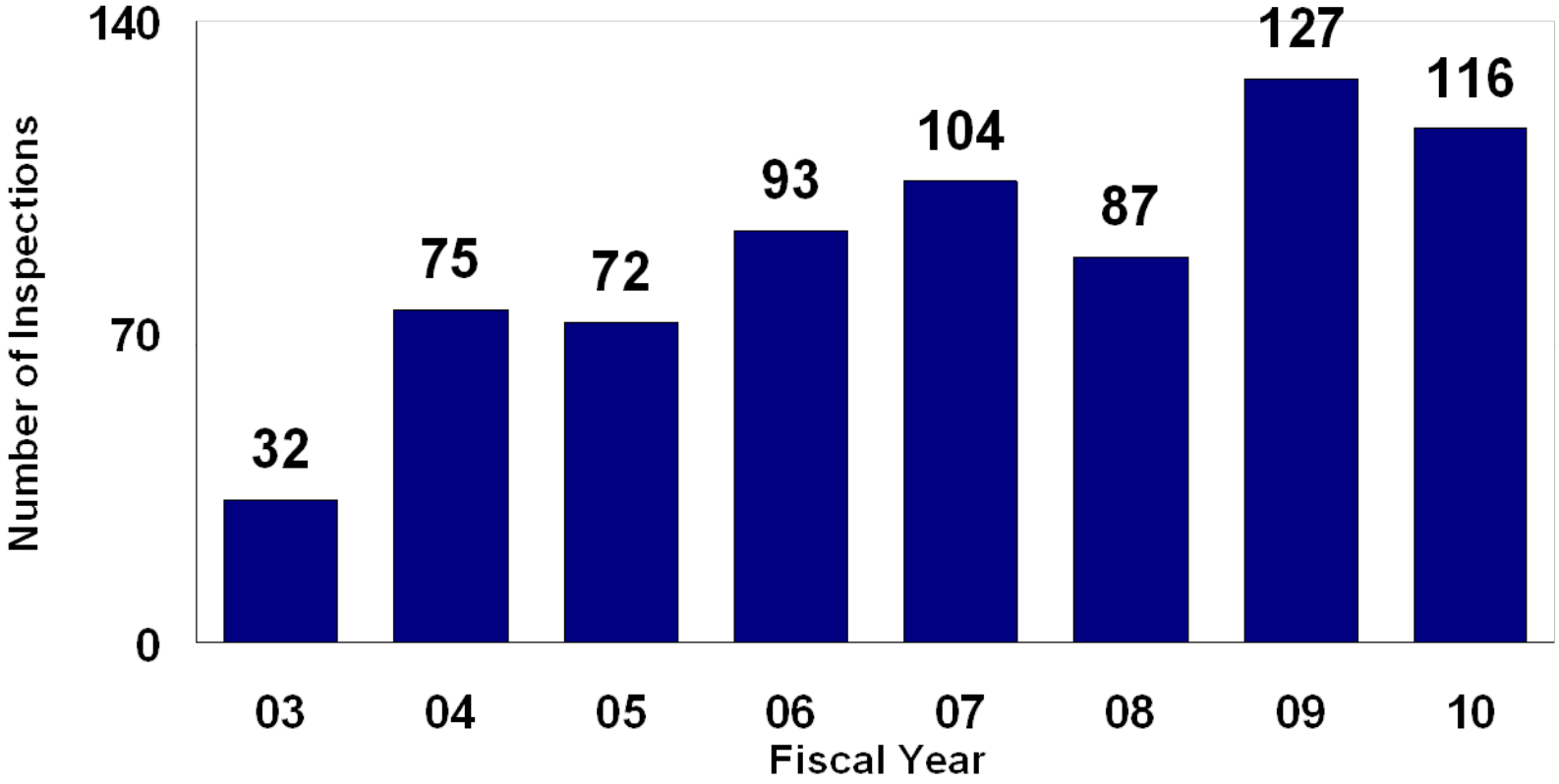
Part 11	ELECTRONIC RECORDS; ELECTRONIC SIGNATURES
Part 50	PROTECTION OF HUMAN SUBJECTS
Part 54	FINANCIAL DISCLOSURE BY CLINICAL INVESTIGATORS
Part 56	INSTITUTIONAL REVIEW BOARDS
Part 312	INVESTIGATIONAL NEW DRUG APPLICATIONS

International Inspections

- 40%-65% of clinical studies investigating FDA-regulated products are conducted outside of the US
- In 2008, 80% of marketing applications received by the FDA contained data from international clinical studies
  - 78% of the participants involved in the studies supporting these applications were enrolled at international sites
  - 54% of the clinical sites conducting these studies were located outside the US

Challenges to FDA's Ability to Monitor and Inspect Foreign Clinical Trials, DHHS, June 2010
http://oig.hhs.gov/oei/reports/oei-01-08-00510.pdf

International Clinical Investigator Inspections (CDER, FY 2003-2010)



http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM256376.pdf

What Do You Think?

Why might a VOICE site be inspected by the FDA?

VOICE-Specific FDA Inspections

- Large volume of work (>5000 participants)
- High enrollment
- Pivotal study for tenofovir gel and supplemental marketing application for Truvada to the FDA
- International sites

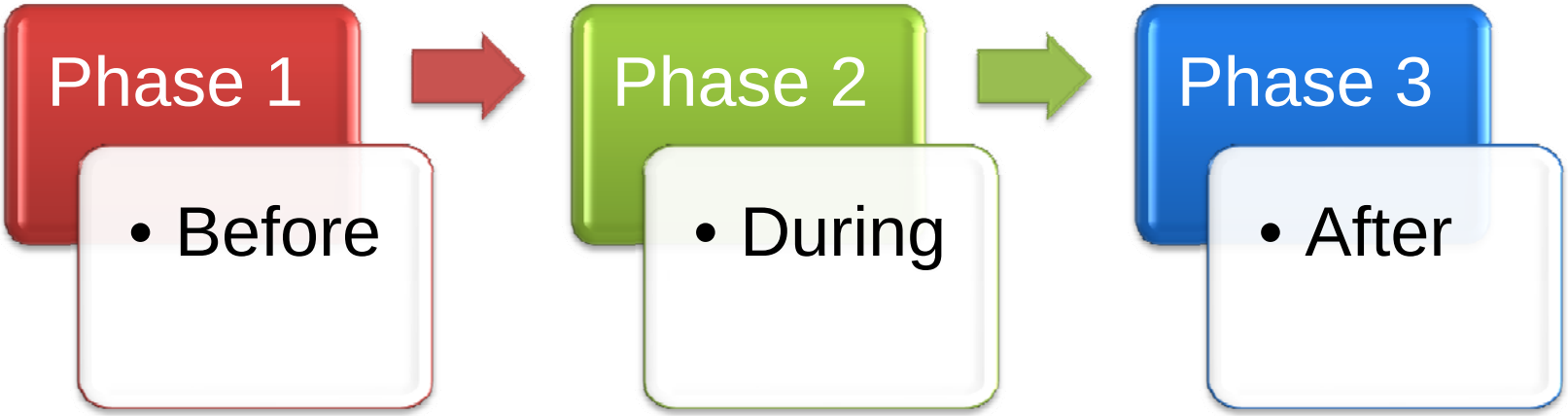
"International inspections are generally assigned when the studies covered are part of a marketing application to FDA and provide data critical to decision-making on product approval."

FDA Compliance Program Guidance Manual

http://www.fda.gov/ICECI/ComplianceManuals/CompliancePrograManual/ucm255614.htm

Overview of the FDA Inspection Process

Three Distinct Phases of an FDA Inspection:



FDA Inspection Process

Role	Task		
	Before	**During**	**After**
Site	Implement inspection preparation activities	Perform assigned roles and responsibilities and provide information to the Inspector	Review observations identified during the inspection and respond to the FDA in writing (if applicable)
Inspector	Review all information regarding the upcoming inspection	Evaluate site practices and procedures to determine compliance with applicable regulations	May or may not issue FDA Form 483 Document inspectional observations in the final report and forward to FDA management
FDA	Determine the site to be inspected	Act as a resource to the on-site Inspector by providing guidance and clarification	Review the final report from the Inspector and determine appropriate actions and/or consequences

Investigator Responsibilities

The Principal Investigator is ultimately responsible for all study-related activities at his or her site, regardless of who has been delegated the various study-related activities

References discussing Investigator Responsibilities:

International Conference on Harmonisation (ICH) Guidelines, E6 – Section 4.0

FDA 21 CFR 312 (Subpart D)

FDA Guidance for Industry – *Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects* (October 2009)
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf

Institutional, local, state, and national regulations

Key Documents

Form FDA 1572 – Statement of Investigator	• The statement completed by the Study Investigator that he/she will abide by the federal guidelines set forth in the Code of Federal Regulations for the use of investigational products in the research setting
Form FDA 482 – Notice of Inspection	• FDA written notice of inspection presented by the FDA Inspector at the beginning of the inspection (for US sites only)
Form FDA 483 – Inspectional Observations	• A list of objectionable conditions or practices observed during the inspection, prepared by the FDA Inspector, and presented to the Study Investigator at the conclusion of an inspection

Key Documents

Establishment Inspection Report	• The report written by the FDA Inspector that describes the observational findings of the inspection
FDA Warning Letter	• A letter that is issued when an Investigator has neglected to take proper corrective action on findings, or one or more observations from the inspection is in violation of laws or regulations
Close-Out Letter	• A letter that may be issued when, based on the FDA's evaluation, the firm has taken corrective action to address the violations contained in the Warning Letter

Inspection Preparedness and Readiness

Inspection Preparedness and Readiness

What is it?

To be inspection ready at all times!

Why now?

So issues are identified and corrected long before the site gets an audit notification

Where to begin?

With an effective quality management plan!

Future Steps

FDA Inspection Checklist

FDA Inspection Preparation Team

Using FDA Resources

U.S. Department of Health & Human Services www.hhs.gov

U.S. Food and Drug Administration

Protecting and Promoting *Your* Health

Search go

A - Z Subject Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

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- Animal & Veterinary
- Cosmetics
- Radiation-Emitting Products
- Tobacco Products

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- E-mail Updates
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FDA Basics

- FDA Basics
- FDA Basics For Industry

Spotlight

- Globalization Report
- FDA Strategic Priorities 2011-2015
- Medical Countermeasures
- HHS 2012 Budget Announced
  - FDA Budget
- Transparency
- Expanded Access to Investigational Drugs
- Strategic Plan for Risk Communication

Science & Research

- Combination Products
- Critical Path Initiative
- Sentinel Initiative
- Clinical Trials
- Pediatrics
- Rare Diseases
- Toxicological Research

More Science & Research

Regulatory Information

- How to Comment on Proposed Regulations
- Code of Federal Regulations
- Dockets Management
- FDA Federal Registers (FR)
- Laws FDA Enforces

More Regulatory Information

About FDA

- FDA Organization

Public Health Focus

- FDA: Apple Juice is Safe To Drink
- Hurricanes: Health and Safety
- Drug Shortages
- Radiation Safety
- Food Safety Modernization Act (FSMA)
- Minority Health
- FDA on Flickr and Facebook
- FDA-TRACK

More Public Health Focus

News & Events

- September 19, 2011 - FDA confirms Listeria monocytogenes on Jensen Farms' Rocky Ford-brand cantaloupes
- September 14, 2011 - FDA warns consumers not to eat Rocky Ford Cantaloupes shipped by Jensen Farms
- September 14, 2011 - FDA establishes foodborne illness outbreak response network
- September 14, 2011 - FDA: Minnesota companies agree to halt sale of amino-acid products with unapproved claims
- September 13, 2011 - FDA investigates multistate outbreak of listeriosis

Newsroom | Meetings | Testimony | Speeches

Report a Problem

- Drugs, Medical Devices... (MedWatch)
- To Report an Emergency
- To Report a Non-Emergency

- Toxicological Research

More Science & Research

Regulatory Information

- How to Comment on Proposed Regulations
- Code of Federal Regulations
- Dockets Management
- FDA Federal Registers (FR)
- Laws FDA Enforces

More Regulatory Information

About FDA

- FDA Organization
- FDA Basics
- Advisory Committees
- International Programs
- Criminal Investigations
- Emergency Preparedness & Response
- Working at FDA
- Training/Continuing Education
- Reports, Manuals & Forms
- Publicaciones en Español

More About FDA

News & Events

- September 06, 2011 - FDA announces new staff training for medical device reviewers
- August 31, 2011 - FDA Commissioner Margaret A. Hamburg's Statement on the Passing of Dr. Charles Edwards
- August 26, 2011 - FDA approves Xalkori with companion diagnostic for a type of late-stage lung cancer
- August 26, 2011 - FDA hurricane preparedness checklist
- August 25, 2011 - FDA: U.S. Marshals seize food products held at North Carolina warehouse

Newsroom | Meetings | Testimony | Speeches

FDA For You

Consumers

- Consumer Updates
- Kids
- Patients and Patient Advocates
- Women's Health
- Minority Health

More Consumers

Industry

- Inspections & Enforcement
- Import Program
- Guidances
- Food Facility Registration
- Prior Notice of Imported Foods

More Industry

Health Professionals

- Drugs
- Medical Devices
- Biologics
- Radiological Health

More Health Professionals

State & Local Officials

- Medical Countermeasures
- HHS 2012 Budget Announced – FDA Budget
- Transparency
- Expanded Access to Investigational Drugs
- Strategic Plan for Risk Communication

Report a Problem

- Drugs, Medical Devices... (MedWatch)
- To Report an Emergency
- To Report a Non-Emergency
- Report Suspected Criminal Activity
- For Industry: Reportable Food Registry

Recalls & Alerts

- Recalls & Safety Alerts
- Warning Letters

More Safety Information

Approvals & Clearances

- Product Approvals

Interactive Media

- Consumer Multi-Media
- Drug Safety Podcasts
- FDA Patient Safety News

More Interactive Media

U.S. Food and Drug Administration · 10903 New Hampshire Ave.
Silver Spring, MD 20993 · 1-888-INFO-FDA (1-888-463-6332)

FDA Website

- Guidance Documents

  Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors: FDA Inspection of Clinical Investigators

  http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126553.pdf

- Database of FDA Form 483 Findings

  http://www.fda.gov/ICECI/EnforcementActions/ucm222557.htm

- Warning Letters

  http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm

- Clinical Trials Section

  http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm

Warning Letter Findings for 2011

10 investigators	You failed to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60]
5 investigators	You failed to personally conduct or supervise the clinical investigation [21 CFR 312.60]
5 investigators	You failed to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)]

Warning Letter Findings for 2011

3 investigators	You failed to report promptly to the IRB all changes in the research activity [21 CFR 312.66]
2 investigators	You failed to obtain informed consent of each subject in accordance with the provisions of 21 CFR part 50 [21 CFR 312.60]
2 investigators	You failed to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)]
1 investigator	You failed to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects [21 CFR 312.62(a)]

Questions?

Section II: OCSO Trend Analyses and Quality Management

This project has been funded in whole or in part with Federal funds from the Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under contract No. N01-AI-50022, entitled HIV Clinical Research Support (CRS) Services.

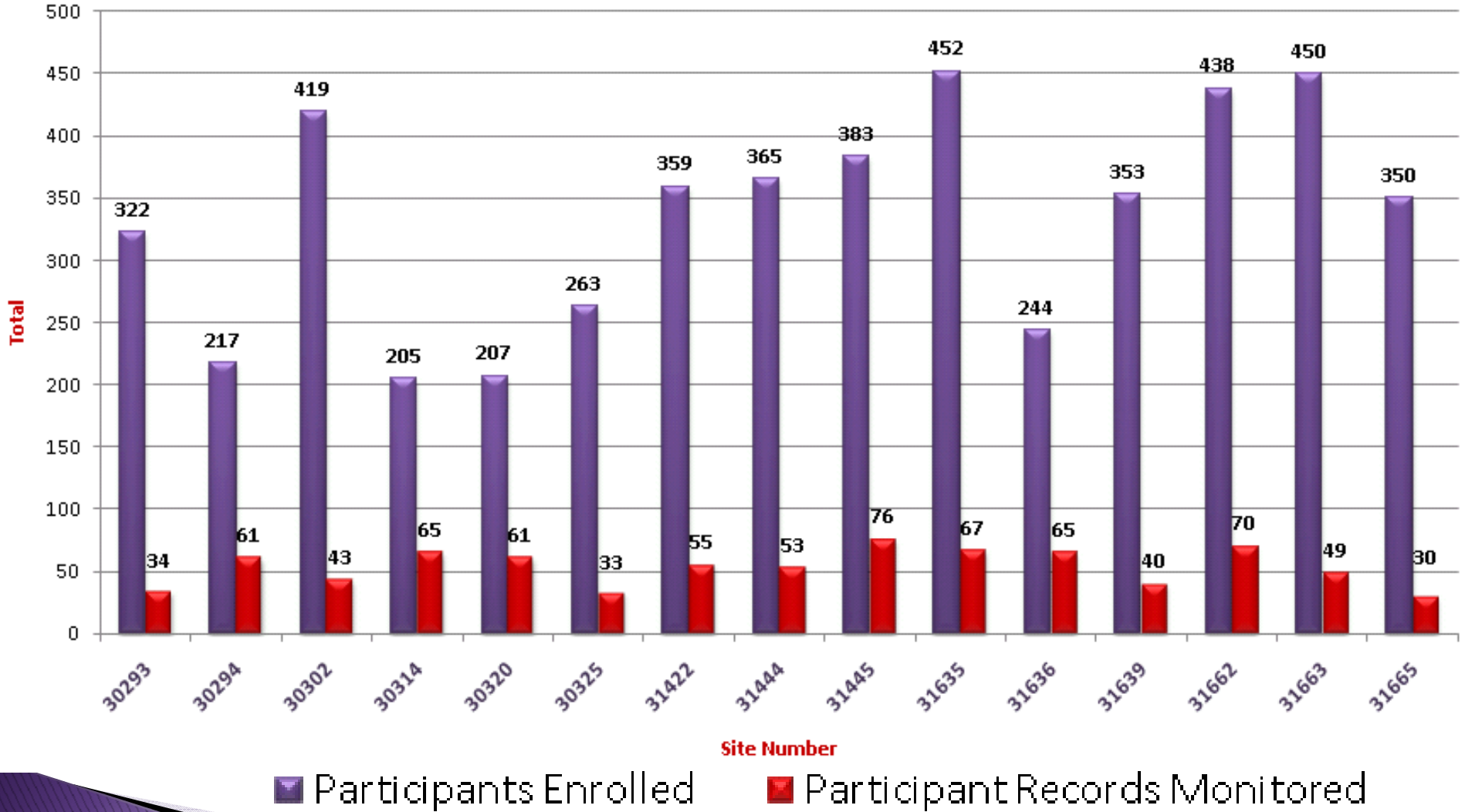
Objectives for Section II

- Identify areas for improvement from the site-specific trend analysis that may require attention prior to an FDA inspection
- Describe the relationship between quality management activities and FDA inspection preparedness
- Identify resources available to the site and how to use them in preparation for an FDA inspection
- Implement quality management techniques that will assist with identification of areas for improvement in preparation for possible FDA inspection

OCSO Trend Analysis Overview

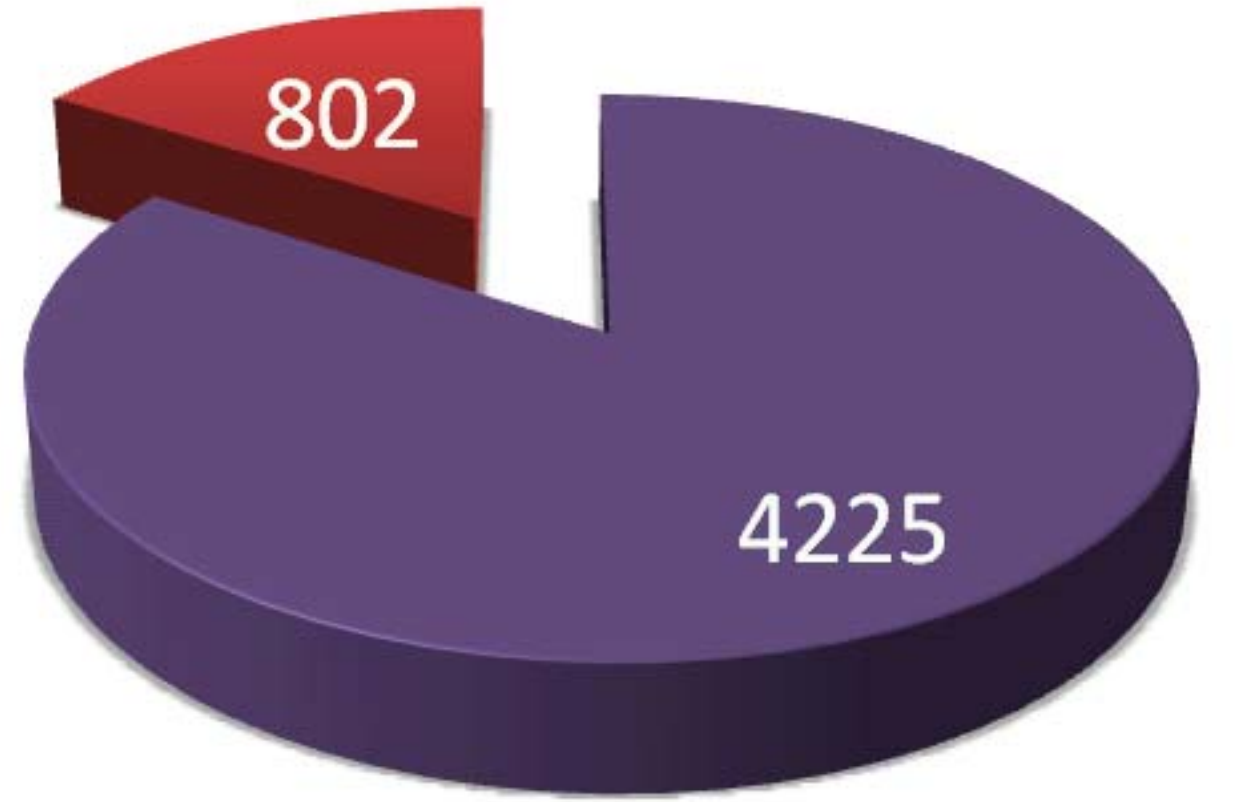
- To identify trends from findings reported in the PPD CSSM Site Monitoring Reports.
  - Including Clinical, Regulatory, Pharmacy and Lab
- To distribute information obtained from the trend analysis for possible corrective and preventive actions, as well as evaluation and modification of current CQMP processes and site-specific SOPs

VOICE Enrolled versus Monitored



Total Sample Size Monitored = 16%

Total Enrollment 5027



What about the other 84%?

Monitoring Trends – As of September 14, 2011

Monitoring Trends	Findings	Warning Letter Examples
Procedural Inadequate Source Documentation (A72)	**676**	Failure to maintain adequate or accurate case histories
Missed Tests/Study Procedures (A14 [inadeq] = 46, A24 [adeq] = 125)	**171**	Failure to complete assessments or procedures as required by the protocol Failure to repeat labs as required by the protocol
Unreported Adverse Events (A62)	**23**	Failure to conduct the studies or ensure they were conducted according to the investigational plans, and to protect the rights, safety, and welfare of subjects
Enrollment Violations (A2)	**4**	Failure to follow the Inclusion/Exclusion criteria or timelines for enrollment as required by the protocol

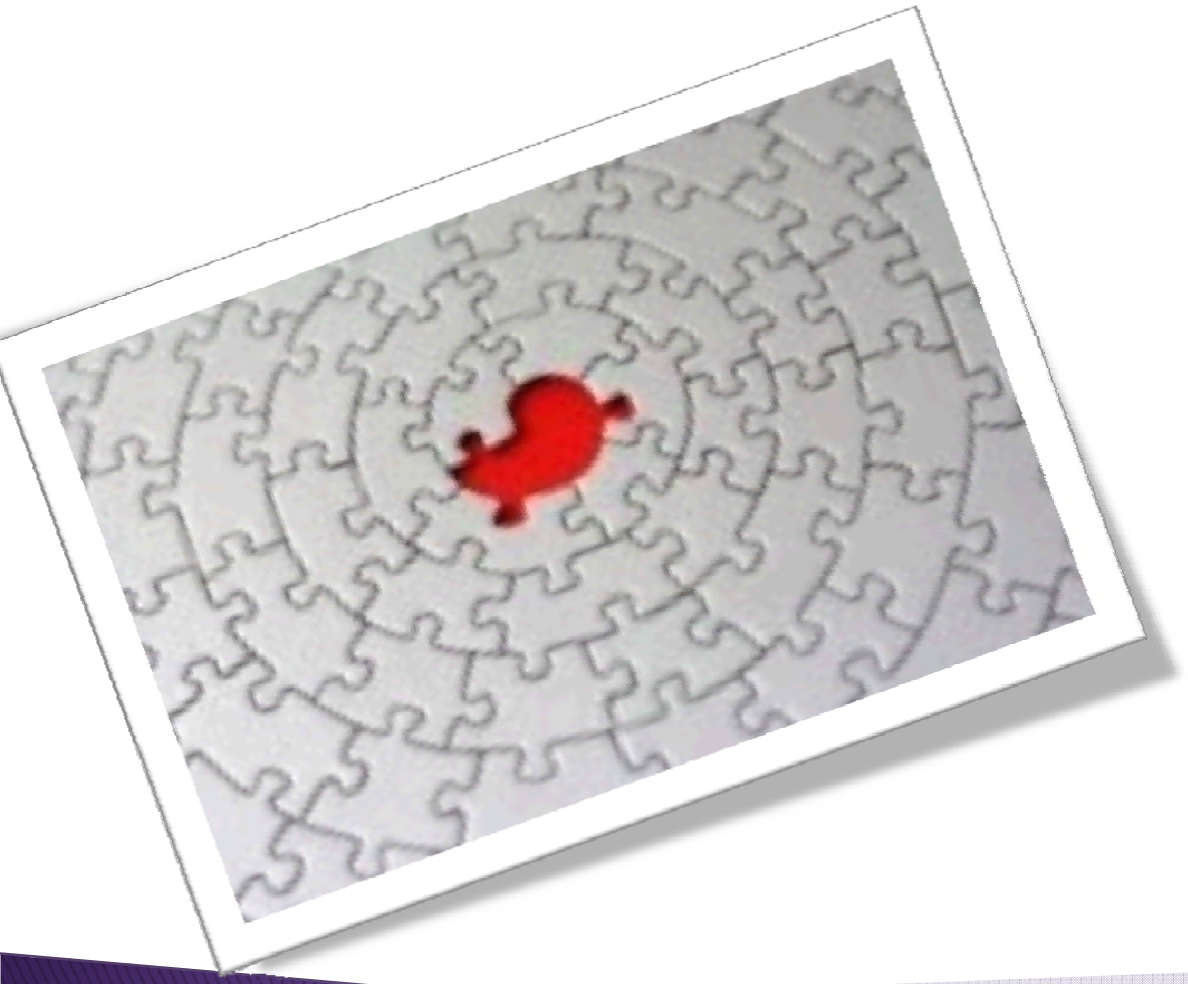
16%

Site Reported Protocol Deviations – As of September 12, 2011

MTN-003 Protocol Deviations	Findings	Warning Letter Examples
Omitted Study Procedures	**83**	Failure to complete assessments or procedures as required by the protocol
Missed Repeat Labs	**32**	Failure to complete assessments or procedures as required by the protocol
Study Product Errors – Study Product Hold (17) Study Product Dispensing (14)	**31**	Failure to adequately document study drug accountability or failure to hold the study drug as required by the protocol
Enrollment Deviations	**26**	Failure to follow the Inclusion/Exclusion criteria or timelines for enrollment as required by the protocol

Objective Check

- Identify areas for improvement from the site-specific trend analysis that may require attention prior to an FDA inspection



Big Picture

How could one define “Quality” in the clinic research setting?

The reliability and confidence of the data collected for the purpose of answering a scientific medical question while complying with ethical principles, clinical research trial requirements, and the laws and regulations governing human subject clinical research.

Protocol

MTN-003

Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate Tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women

Microbicide Trials Network

Sponsored by:
Division of AIDS, US National Institute of Allergy and Infectious Diseases
US National Institute of Child Health and Human Development
US National Institute of Mental Health
US National Institutes of Health

Grant #:
5-U01-AI068633-05

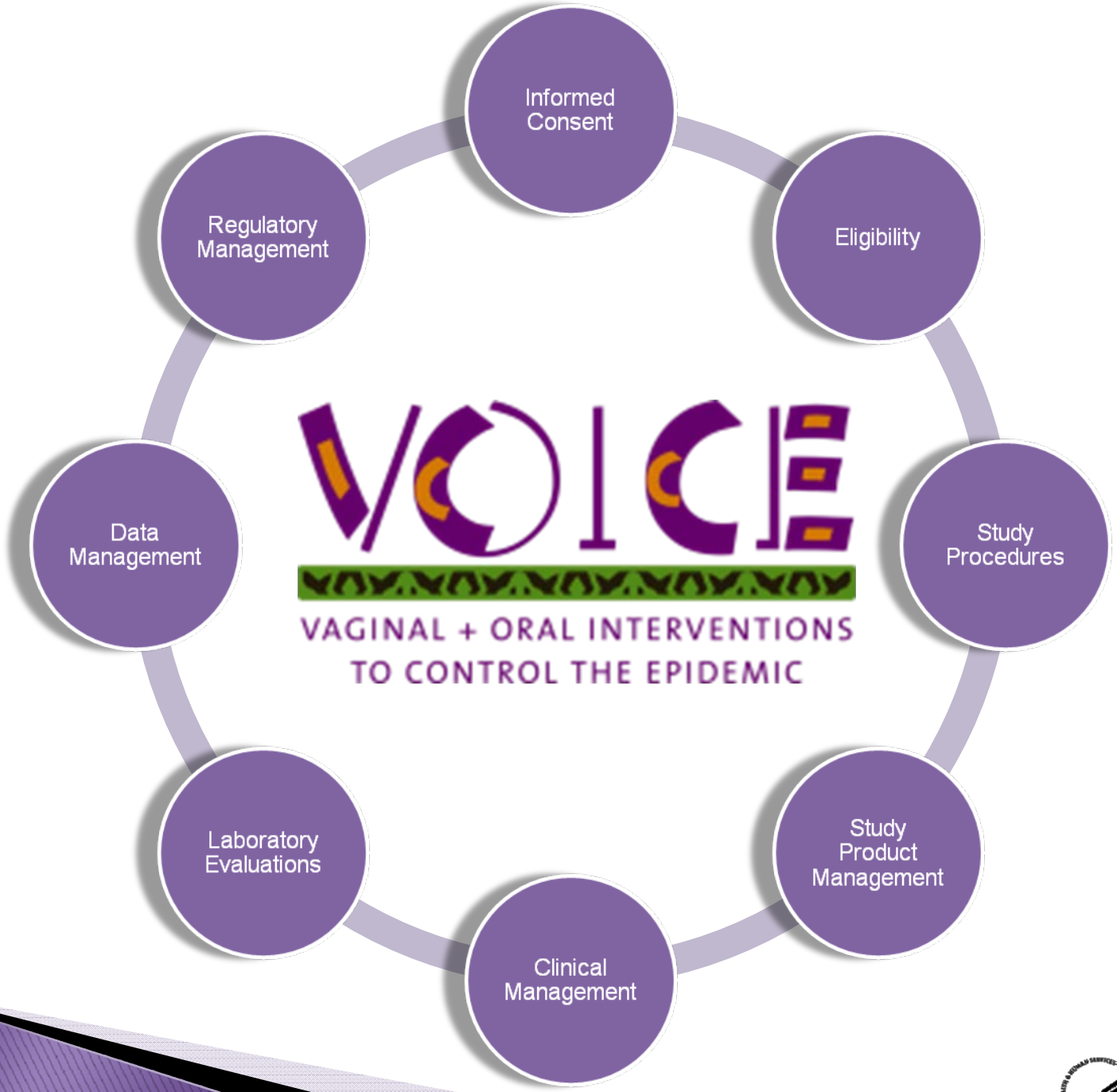
DAIDS Protocol #: 10622

Co-sponsored by:
CONRAD
Gilead Sciences, Inc.

IND# 55,690

Protocol Chairs:

Zvavahera Mike Chirenje, MD, FRCOG
Jeanne Marrazzo, MD, MPH


Informed Consent
Eligibility
Study Procedures
Study Product Management
Clinical Management
Laboratory Evaluations
Data Management
Regulatory Management
VOICE
VAGINAL + ORAL INTERVENTIONS
TO CONTROL THE EPIDEMIC

Ethical Principles

Laws and Regulations

ICH GCP/GLP

Sponsor Requirements

Ethical Principles

Laws and Regulations

ICH GCP/GLP

Sponsor Requirements

NIAID/DAIDS

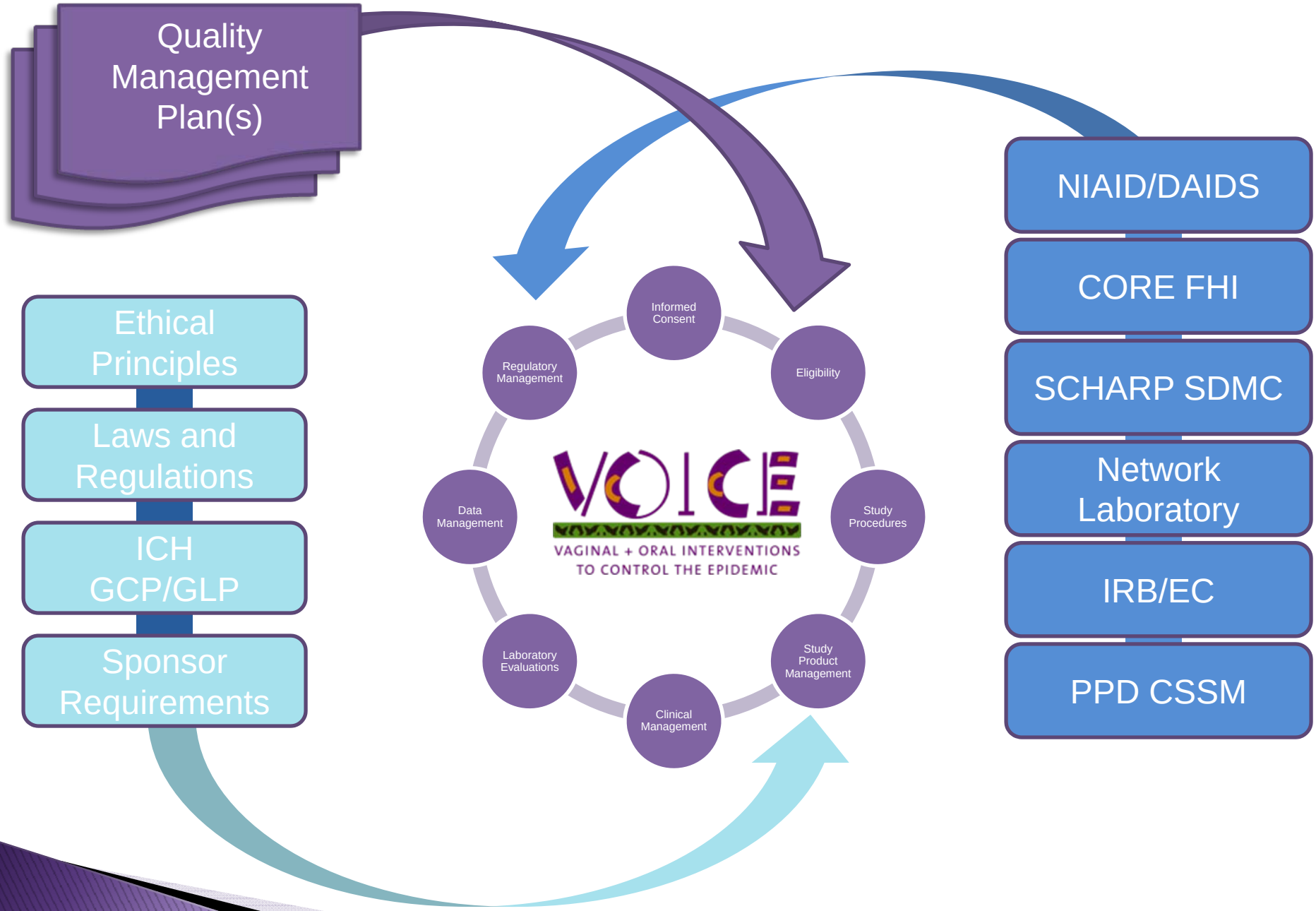
CORE FHI

SCHARP SDMC

Network Laboratory

IRB/EC

PPD CSSM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MTN/CORE FHI
SCHARP SDMC
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IRB/EC
PPD CSSM
FDA Inspection Preparedness


Quality Management
Quality Control
Quality Assurance
Quality Management Plan(s)

Basic Elements of a Quality Management Plan

- Responsibilities
- Quality Control
- Quality Assurance
- Key Quality Indicators
- Tools
- Evaluation
- Reporting

Benefits to Quality Management

To ensure participant safety

Verify accuracy of data; reduce error rates

Identify areas in need of corrective action

Assure compliance with study requirements

Prepared for an external audit, monitoring visit, or FDA Inspection

Objective Check

- Describe the relationship between quality management activities and FDA inspection preparedness

Roles and Responsibilities

Investigator of Record

An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement [FDA Form 1572], the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of the subjects under the investigator's care; and for the control of the drugs under investigation.

21 CFR 312.60

Structure

Investigator of Record

Clinical Research Site

Laboratory

Pharmacy

Study Team

Investigator of Record

Clinical Research Site

Clinical Research Coordinator

Laboratory

Laboratory Director

Pharmacy

Pharmacist of Record

Quality Management

Investigator of Record

Informed Consent

Eligibility

Study Procedures

Study Product Management

Clinical Management

Laboratory Evaluations

Data Management

Regulatory Management

VOICE

VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC

QMP

Clinical Research Site

QMP

Laboratory

QMP

Pharmacy

References

Clinical

DAIDS Policy: Requirements for Clinical Quality Management Plans

MTN-003 SSP Manual: Section 16.1 Site Quality Management Plans

Pharmacy

Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks: Responsibilities of the Pharmacist of Record – Quality Management

Laboratory

DAIDS Guidelines for Good Clinical Laboratory Practice Standards: Quality Management

HIV Prevention Trials Network (HPTN)-MTN Laboratory Manual: MTN Laboratory Quality Assessment and Quality Control Program

Cross-functional Communication Example

During a periodic pharmacy quality assurance activity, the reviewer identifies multiple prescriptions written and signed by an unauthorized prescriber in the clinic. These prescriptions were subsequently filled by pharmacy staff.

Problem 1: Unauthorized Prescriber - Clinic

Problem 2: Filling prescriptions from unauthorized prescriber - Pharmacy

Problem 3: Communication – Clinic and Pharmacy

Key Quality Indicators

Key Quality Indicators Defined

Performance **areas** and **activities** that are vital to compliance with accepted standards of performance.

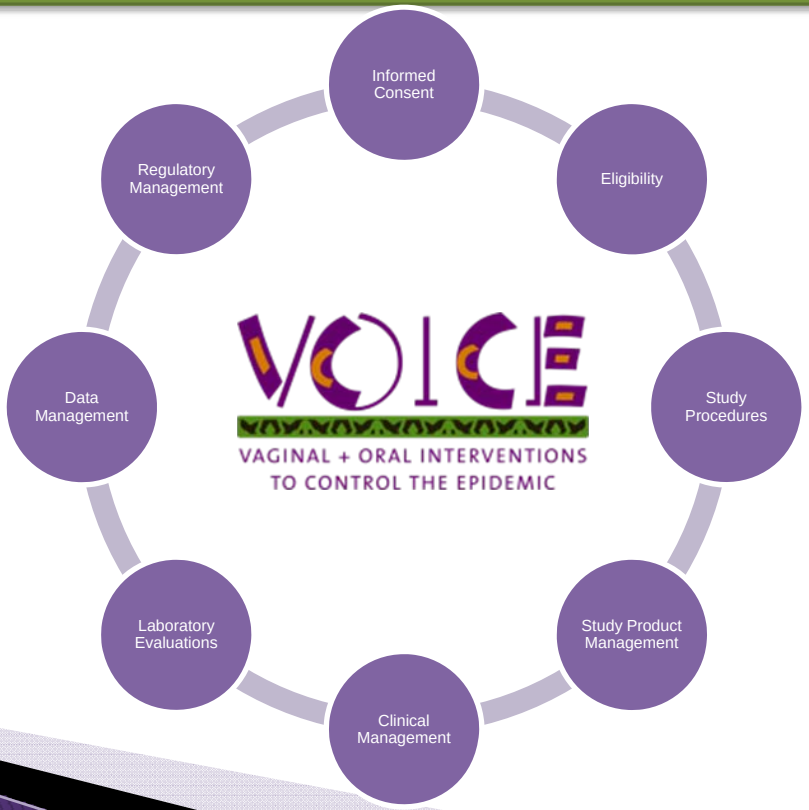
Measurable

Standard/Threshold


Informed Consent Form and Processes
IRB/EC Approval
Inclusion Exclusion Criteria
Informed Consent
Regulatory Management
Eligibility
Data Management
Study Procedures
VOICE
VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC
DataFax Submission
Missed Tests/ Procedures
Laboratory Evaluations
Study Product Management
Hematology Tests
Clinical Management
Study Product Accountability
AE's, SAE's, EAE's

Key Quality Indicators Activity

Based on the OCSO Trend Analysis, what are some additional KQIs that might be considered?



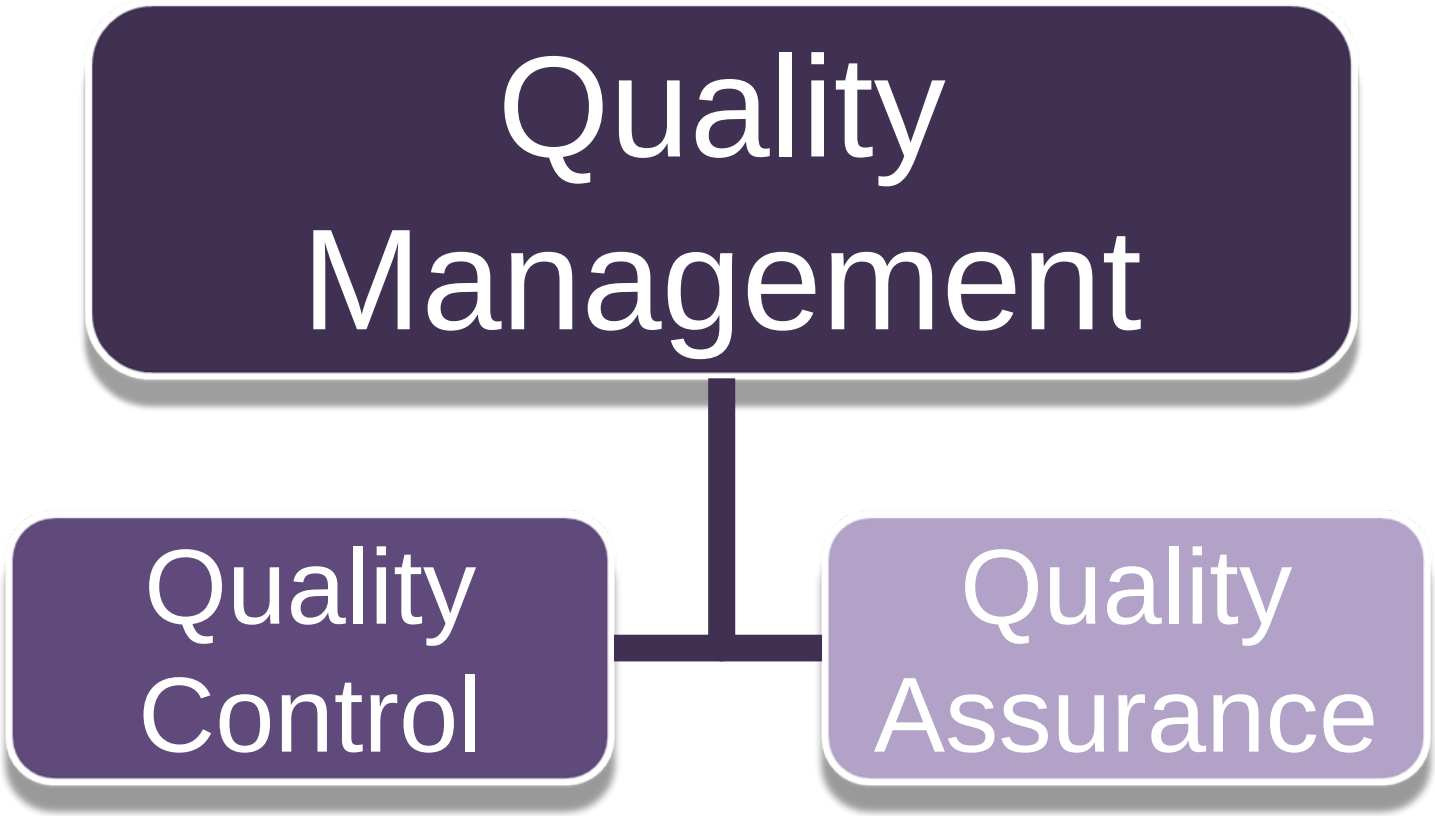
10:00am Break
(30 Minutes)

Quality Management Implementation and Documentation

MTN-003

11.3 Quality Control and Quality Assurance

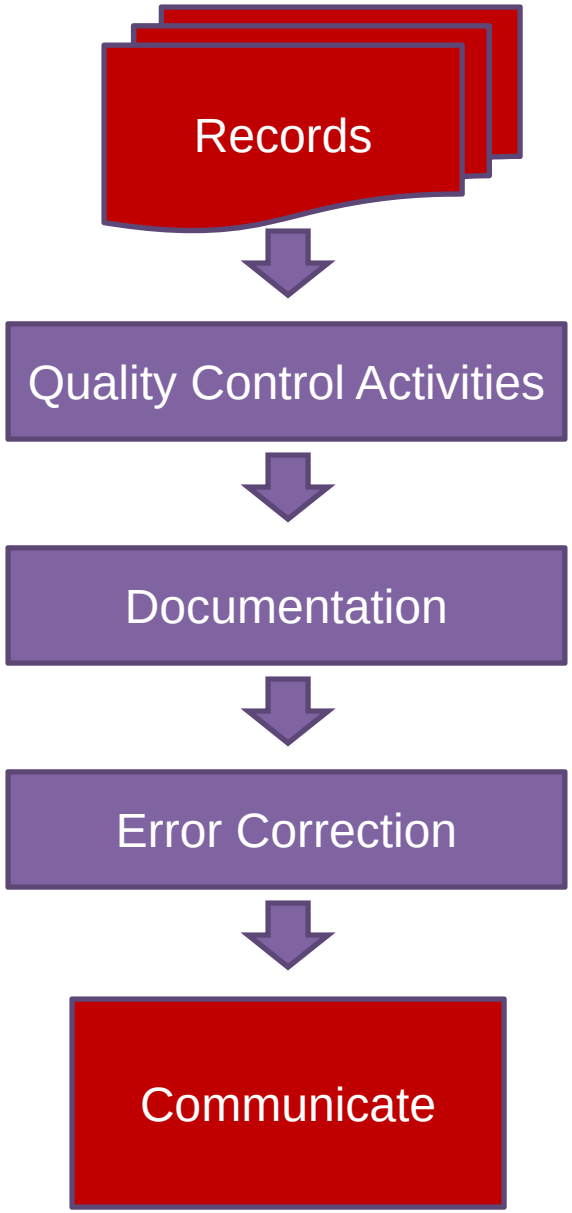
All study sites will conduct quality control and quality assurance procedures in accordance with Requirements for Clinical Quality Management Plans at DAIDS Funded and/or Supported Clinical Research Sites (http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/qmppolicy.pdf)


Quality Management
Quality Control
Quality Assurance

Quality Control

Sample Size
100%

Frequency
Real-time, daily



What will be reviewed? Consider Key Quality Indicators.

What is the step-by-step process for completing QC activities?

How will errors be documented for analysis?

How will errors be corrected?

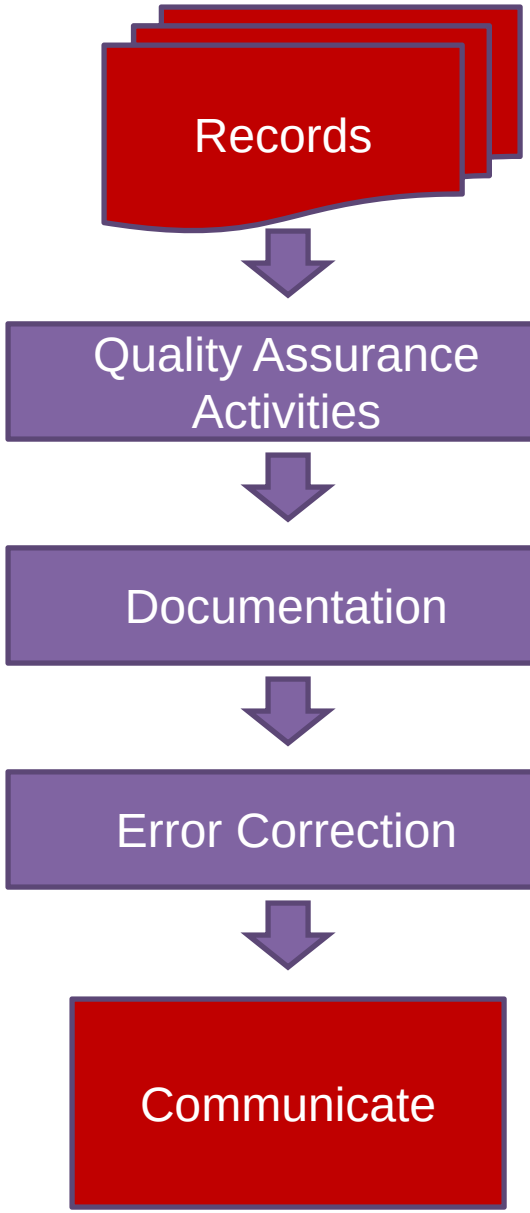
How will the errors, corrective actions, and preventive actions be communicated?

Quality Assurance

Sample Size
Variable

Frequency
Periodic

RETROACTIVE REVIEW



What will be reviewed? Consider Key Quality Indicators.

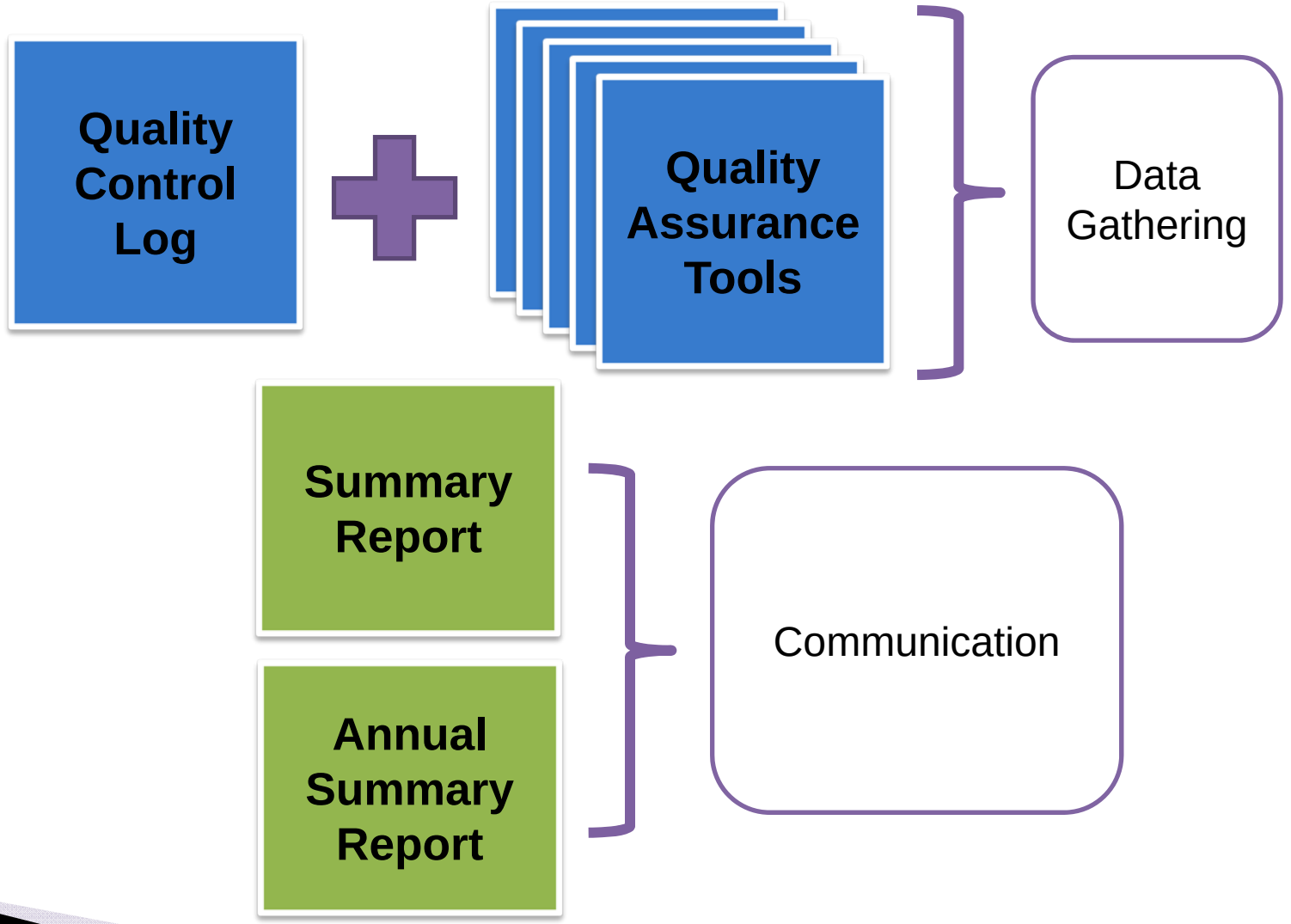
What is the step-by-step process for completing QA activities?

How will errors be documented for analysis?

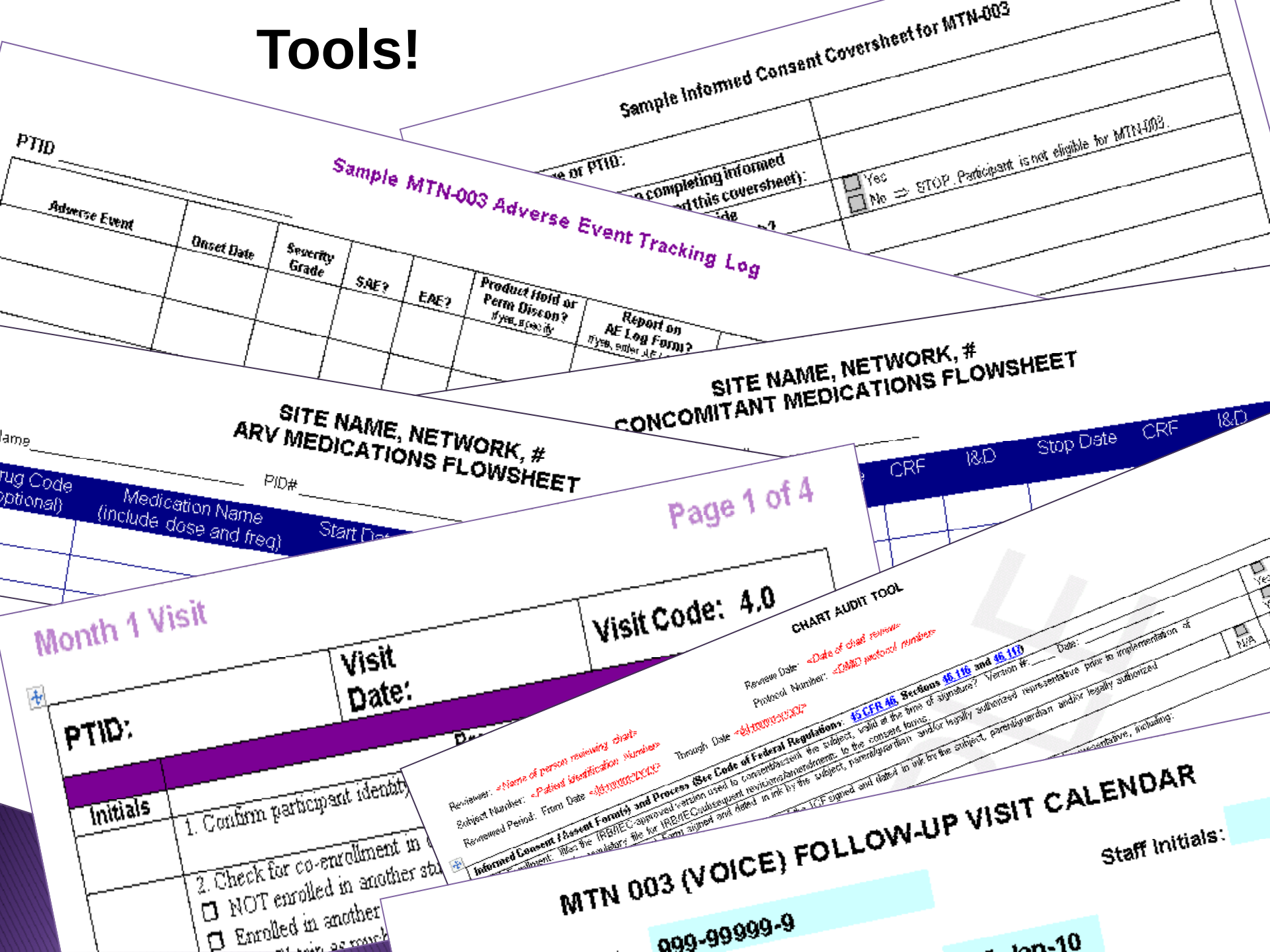
How will errors be corrected?

How will the errors, corrective actions, and preventive actions be communicated?

Internal Quality Management Reporting Structure



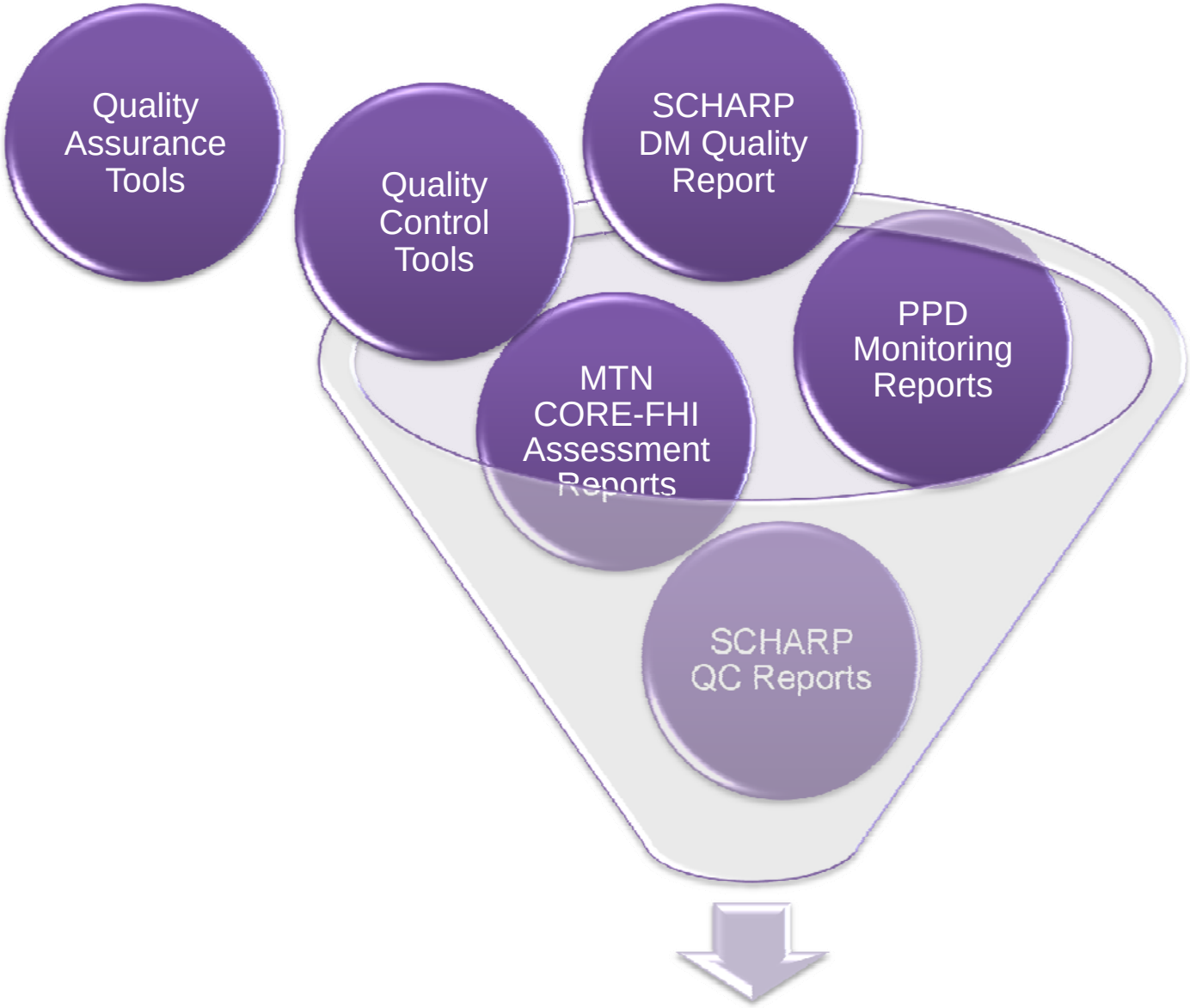
Tools!


Sample Informed Consent Coversheet for MTN-003
PTID
Sample MTN-003 Adverse Event Tracking Log
Adverse Event
Onset Date
Severity Grade
SAE?
EAE?
Product Hold or Perm Discon?
Report on AE Log Form?
SITE NAME, NETWORK, #
ARV MEDICATIONS FLOWSHEET
PID#
Medication Name (include dose and freq)
SITE NAME, NETWORK, #
CONCOMITANT MEDICATIONS FLOWSHEET
Stop Date
CRF
I&D
Page 1 of 4
Month 1 Visit
PTID:
Visit Date:
Visit Code: 4.0
Initials
1. Confirm participant identity
2. Check for co-enrollment in
NOT enrolled in another
Enrolled in another
CHART AUDIT TOOL
Reviewer: <Name of person reviewing chart>
Subject Number: <Patient identification Number>
Reviewed Period: From Date <dd/mmm/yyyy>
Through Date <dd/mmm/yyyy>
Review Date: <Date of chart review>
Protocol Number: <DAIDS protocol number>
Informed Consent / Assent Form(s) and Process (See Code of Federal Regulations: 45 CFR 46, Sections 46.116 and 46.117)
MTN 003 (VOICE) FOLLOW-UP VISIT CALENDAR
Staff Initials:
999-99999-9

MTN-003 Study Implementation Materials

Visit Checklists		
01: Screening, Part 1	2010-Apr-16	97.5 KB
02: Between Screening Part 1 and Screening Part 2 Worksheet	2010-Apr-16	63 KB
03: Screening, Part 2	2010-Apr-16	89.5 KB
04: Screening, Pelvic Exam	2010-Apr-16	70.5 KB
05: Between Screening Part 2 and Enrollment Worksheet	2010-Apr-16	67.5 KB
06: Enrollment	2010-Apr-16	129.5 KB
07: Month 1 Visit	2010-Apr-16	114 KB
08: Monthly Visit	2010-Apr-16	109.5 KB
09: Quarterly Visit	2010-Apr-16	110.5 KB
10: Follow-up Pelvic Exam	2010-Apr-16	67 KB
11: Semi Annual Visit	2010-Apr-16	118.5 KB
12: Annual Visit	2010-Apr-16	95 KB
13: Product Use End Visit (PUEV)	2010-Apr-16	107 KB
14: Termination/Study Exit Visit	2010-Apr-16	98 KB
15: Interim Vist Checklists	2010-Aug-16	75.5 KB
16: HIV Sample 2 Visit Checklist	2010-Aug-16	43.5 KB
17: Post-Seroconversion Checklist	2011-Mar-21	57.21 KB

Trending



Quality Management Summary Report Tool

Communicate

Objective Check

- Identify resources available to the site and how to use them in preparation for an FDA inspection

Trending Activity

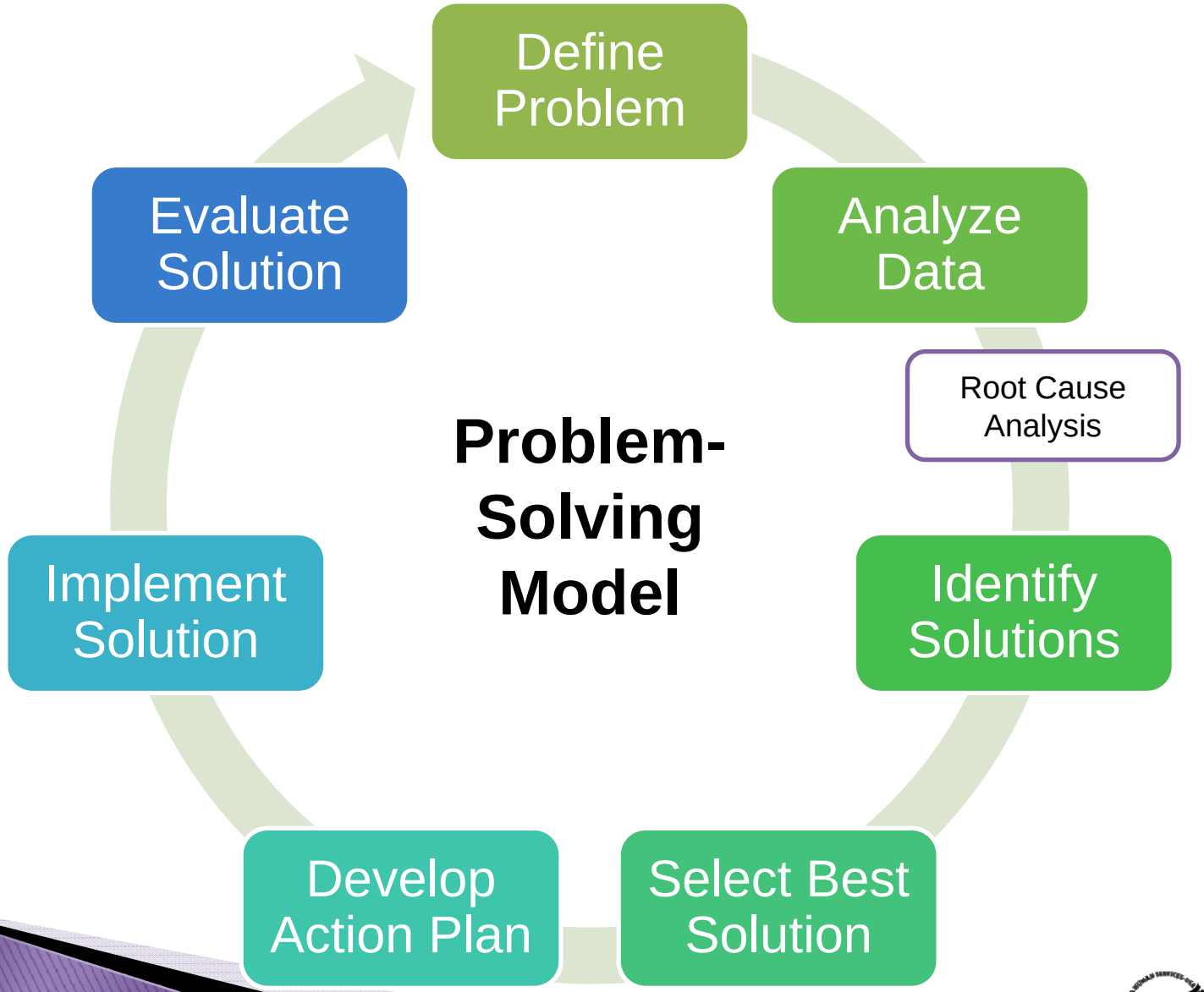
The monitoring visit has just concluded, and the monitor has left you, the Quality Manager, with completed copies of the Monitor Record Review Tools for each participant record reviewed. The Monitor Record Review Tools document the observations noted by the monitor for each participant record reviewed during the visit. As the Quality Manager, you will now compare observations from these monitoring tools, the Quality Management Chart Review Tools, and the Quality Control Log in an effort to identify observational trends.

Trending Activity Matrix

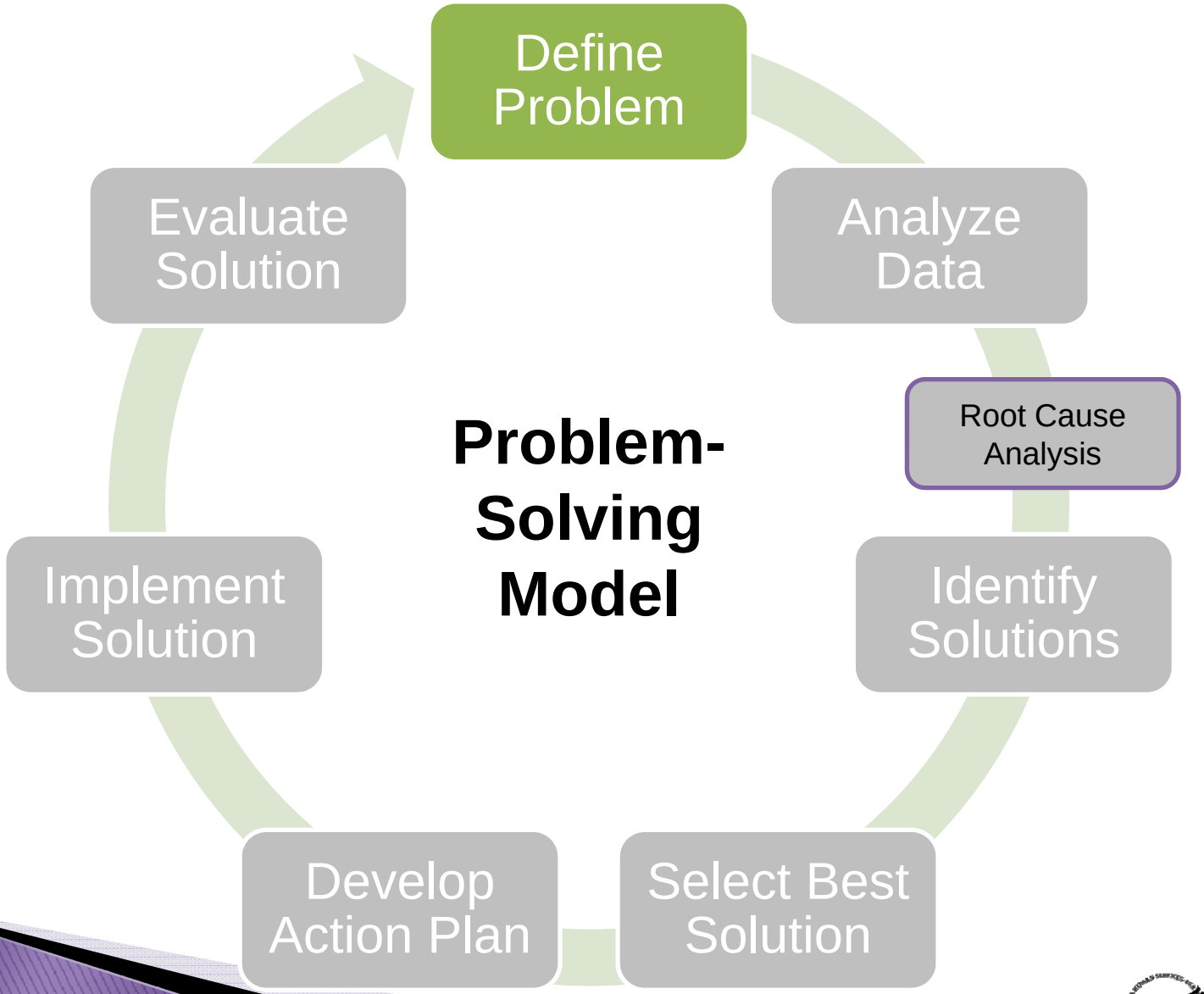
Monitor (3)	Quality Control (10)	Quality Assurance (6)
555100117	555100117	555100117
555100119	555100119	555100119
555100127	555100127	555100127
	555100101	555100101
	555100123	555100123
	555100107	555100129
	555100125	
	555100113	
	555100121	
	555100115	

Problems and Trends Found

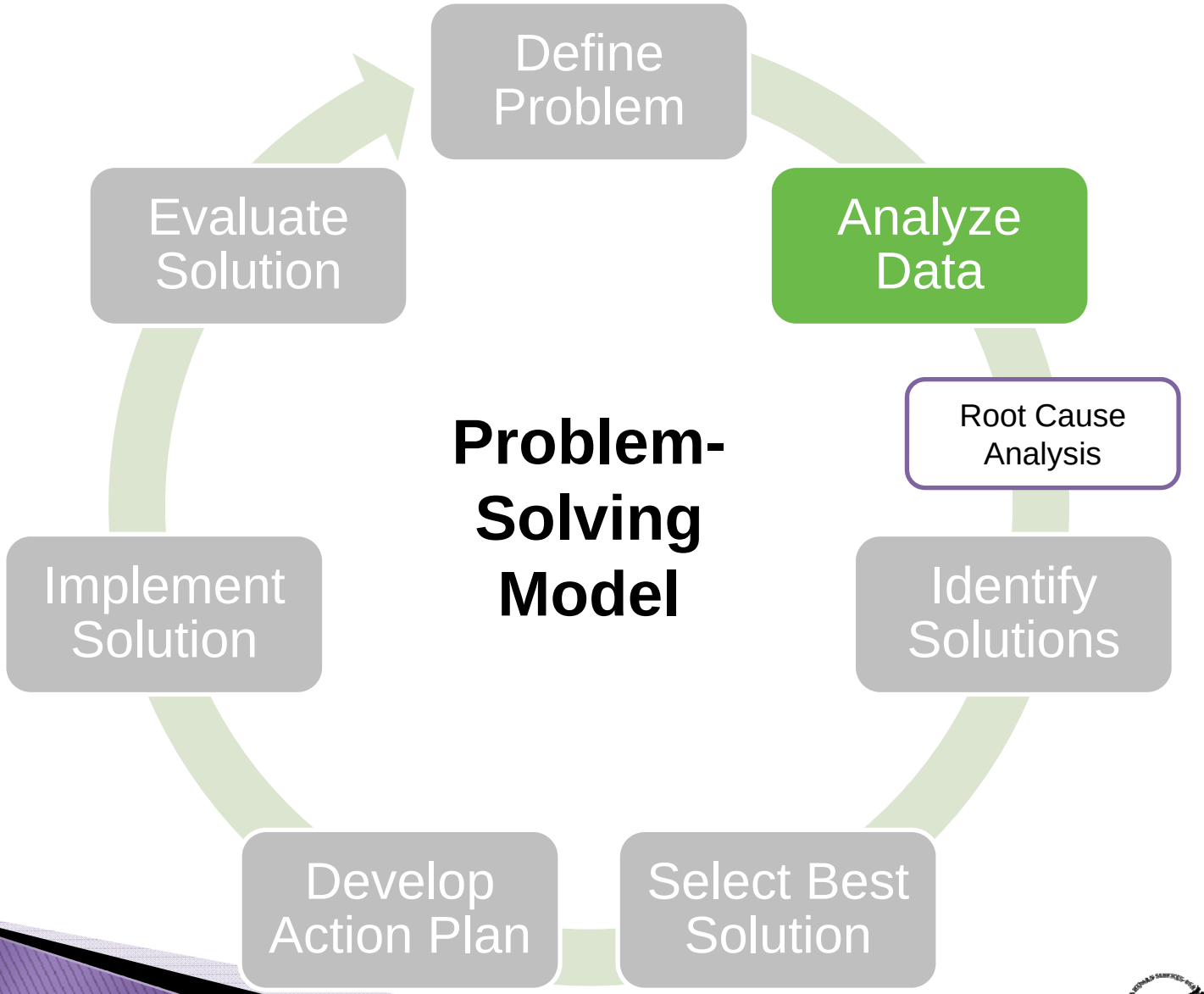
Now What?


Define Problem
Analyze Data
Root Cause Analysis
Identify Solutions
Select Best Solution
Develop Action Plan
Implement Solution
Evaluate Solution
Problem-Solving Model

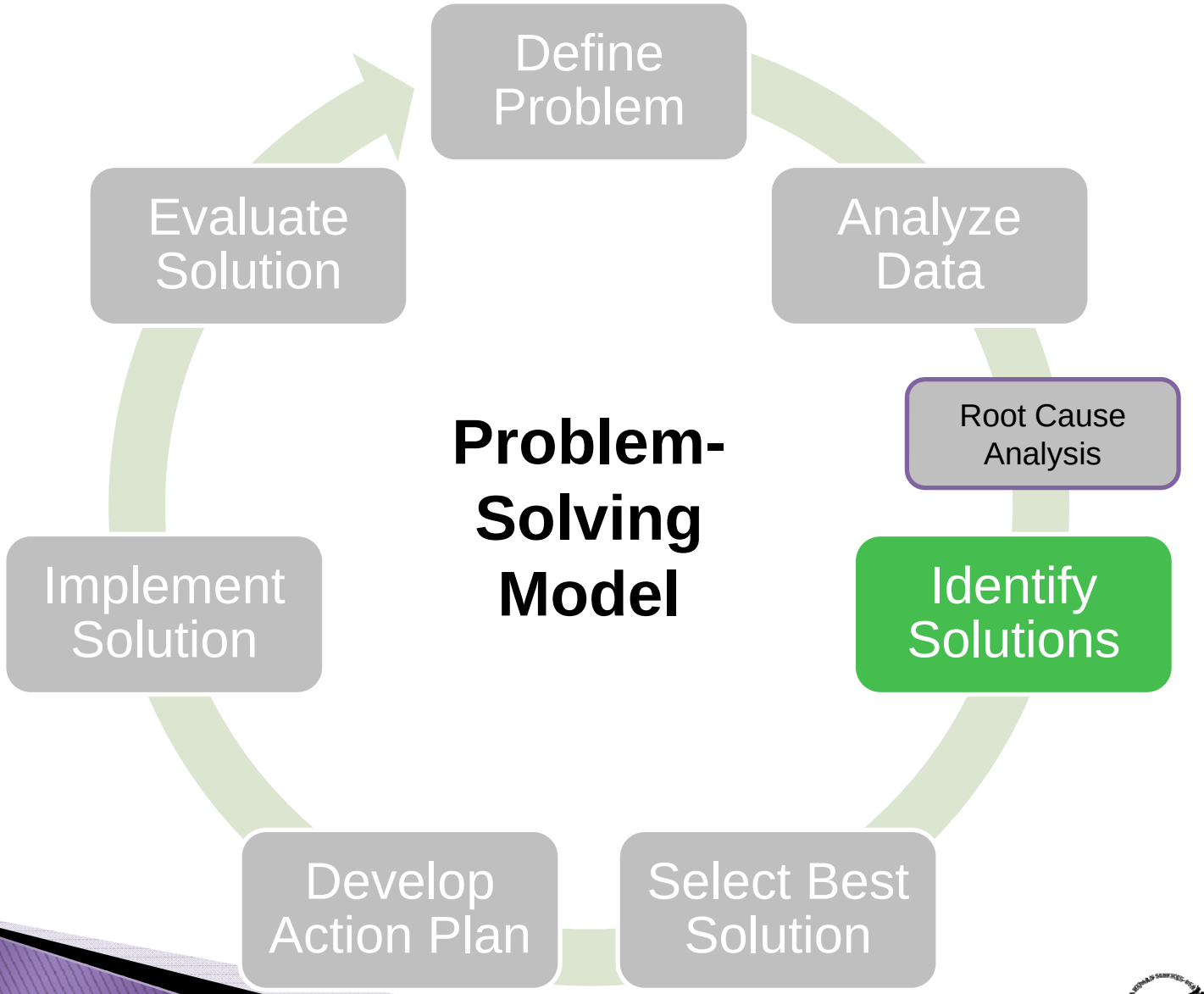
Define Problem



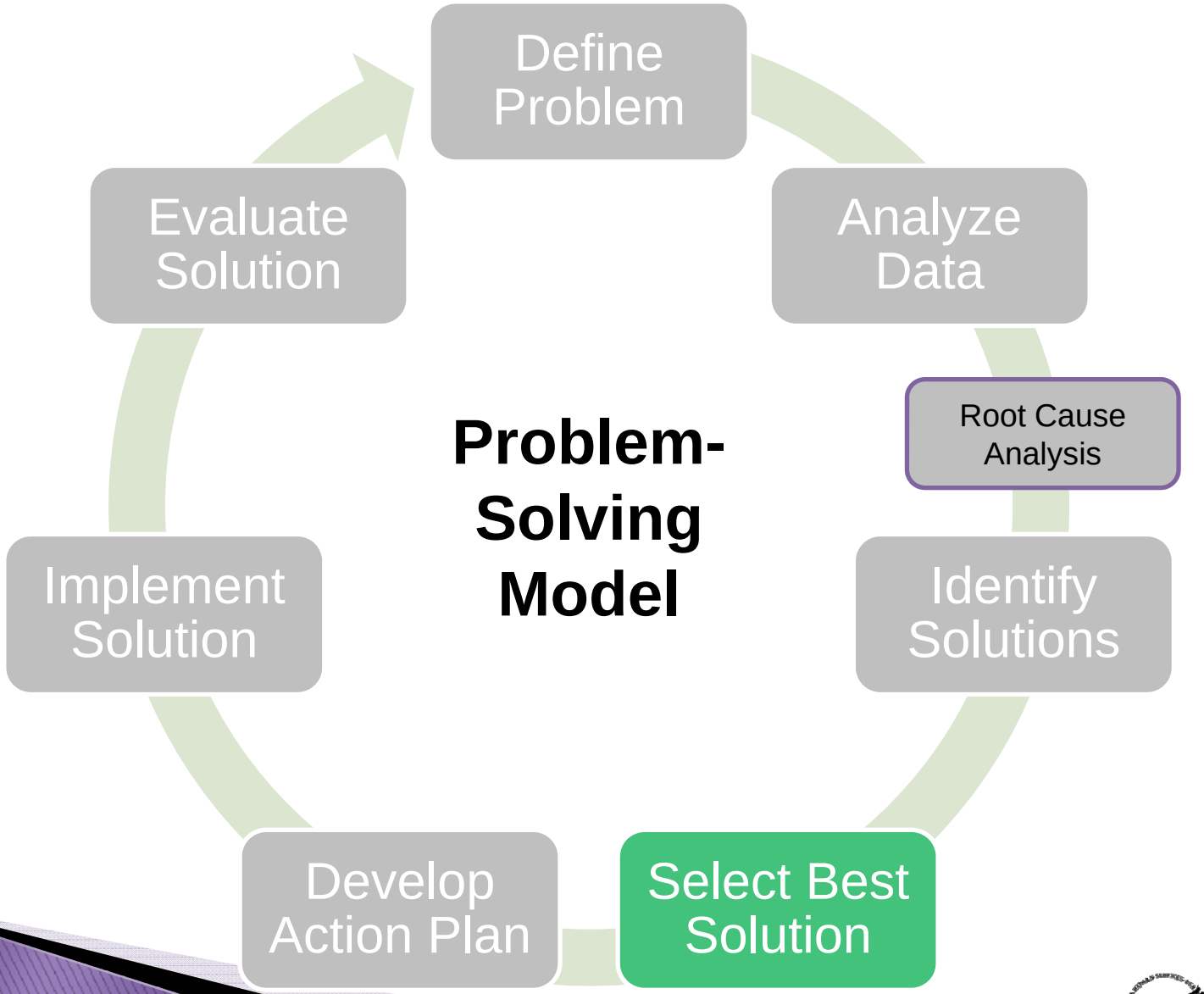
Analyze Data



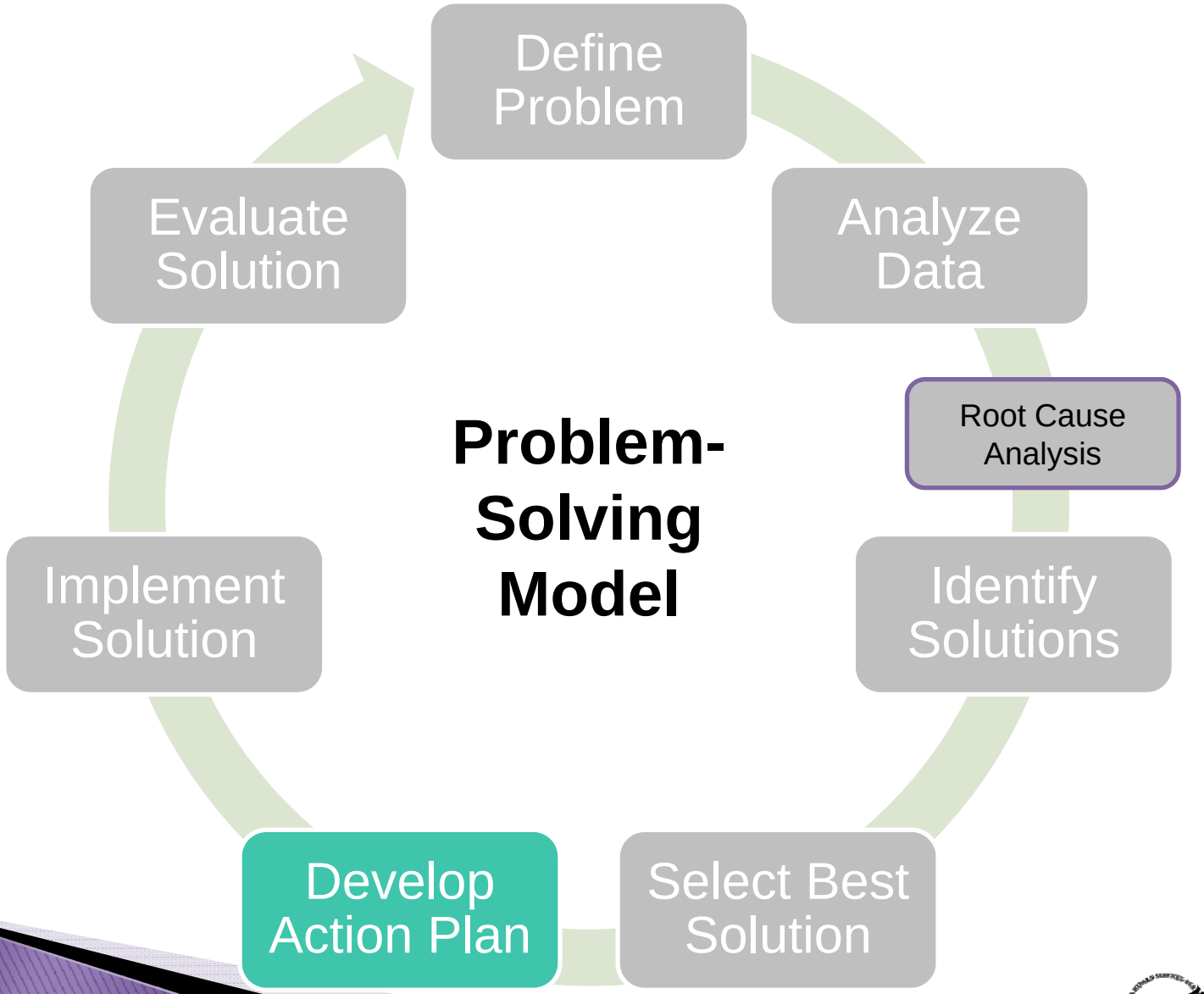
Identify Solutions



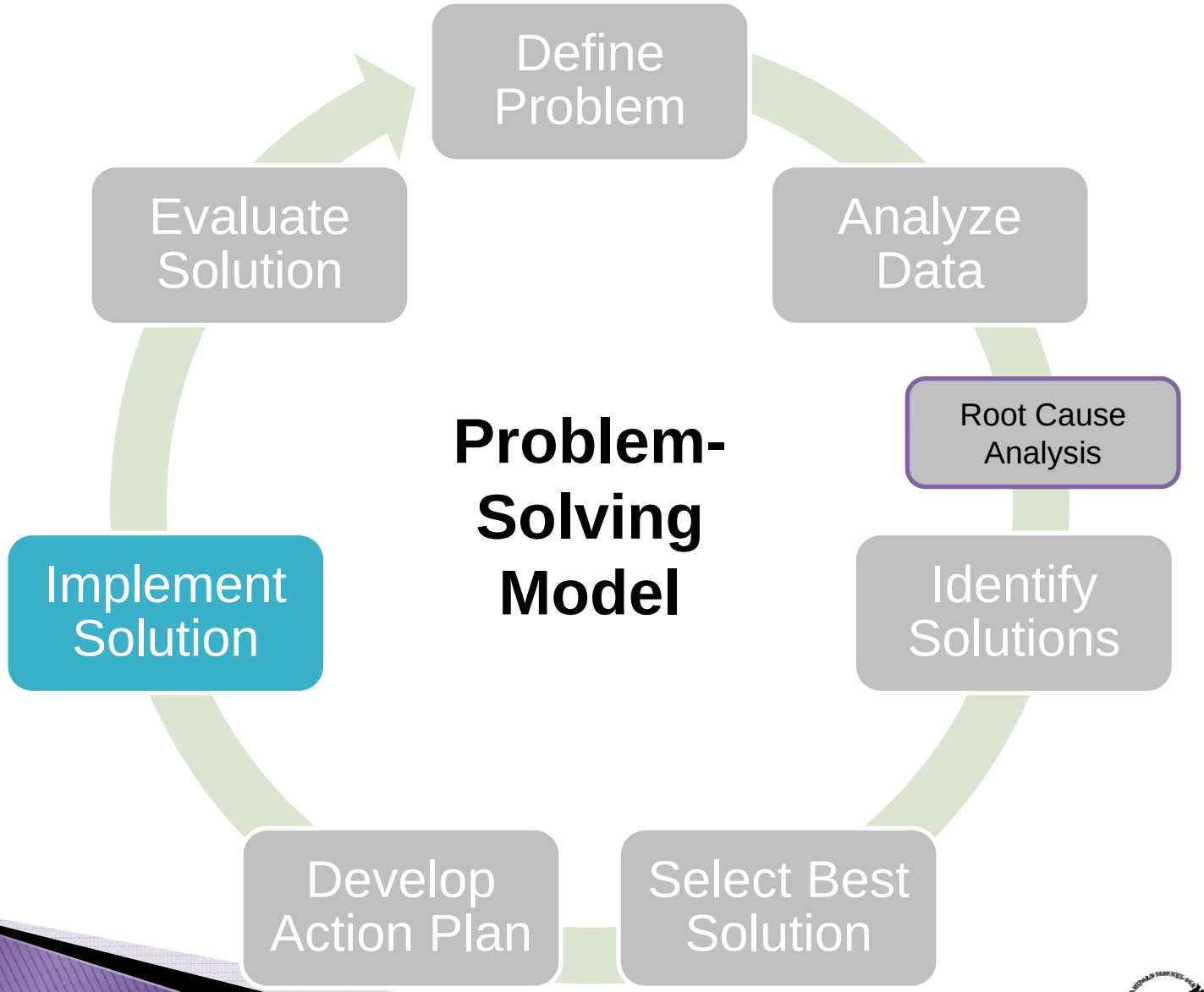
Select Best Solution



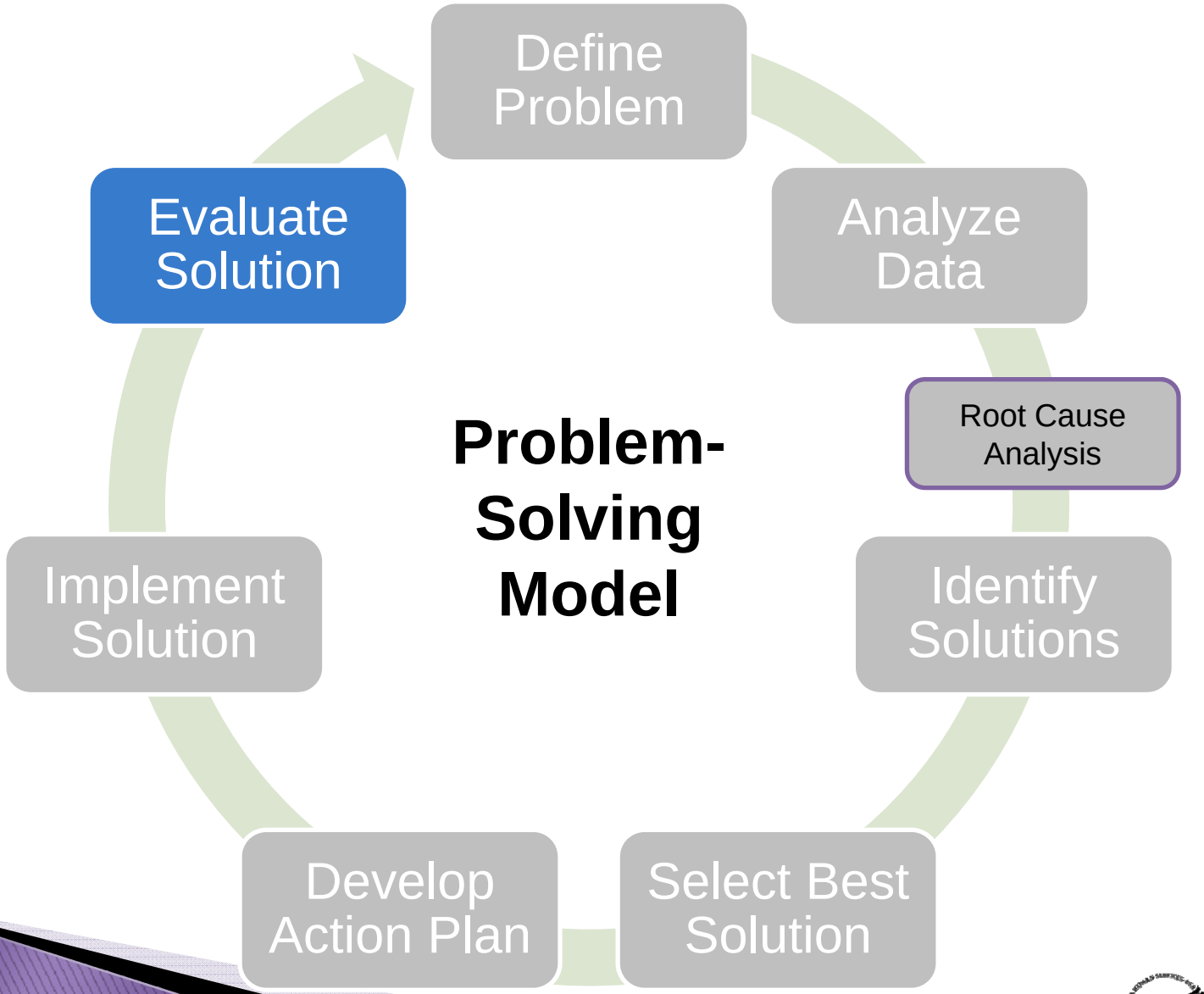
Develop Action Plan



Implement Solution



Evaluate Solution



Quality Management Plan Evaluation

Immediate

Periodic

Annual

Objective Check

- Implement quality management techniques that will assist with identification of areas for improvement in preparation for possible FDA inspection

Quality Management Plan(s)

Investigator of Record

Quality

Informed Consent

Eligibility

Study Procedures

Study Product Management

Clinical Management

Laboratory Evaluations

Data Management

Regulatory Management

VOICE

VAGINAL + ORAL INTERVENTIONS TO CONTROL THE EPIDEMIC

Management

Clinical Research Site

Laboratory

Pharmacy

FDA Inspection Preparedness

Questions?

Next Steps

Donna Germuga, DAIDS OCSO

Next Steps

- Modify CQMP as needed
  - Conduct retrospective reviews on KQIs
  - Develop corrective action as needed
  - Re-evaluate corrective action-IS IT WORKING?
  - DOCUMENT all QC/QA activities

**If currently no significant trends or findings, then continue internal QA/QC activities and proactively identify and resolve any issues or trends in preparation for FDA audit. Good Work!!!*

Next Steps

- Initiate FDA inspection checklist
  - Establish FDA inspection prep team (clinical, lab, pharmacy, regulatory, QA/QC)
    - Appoint one person to act as central “Coordinator”
    - Delegate individual/s to oversee completion of each section
    - Schedule regular meetings to discuss progress, findings
    - Develop a systematic plan and timeline for completion

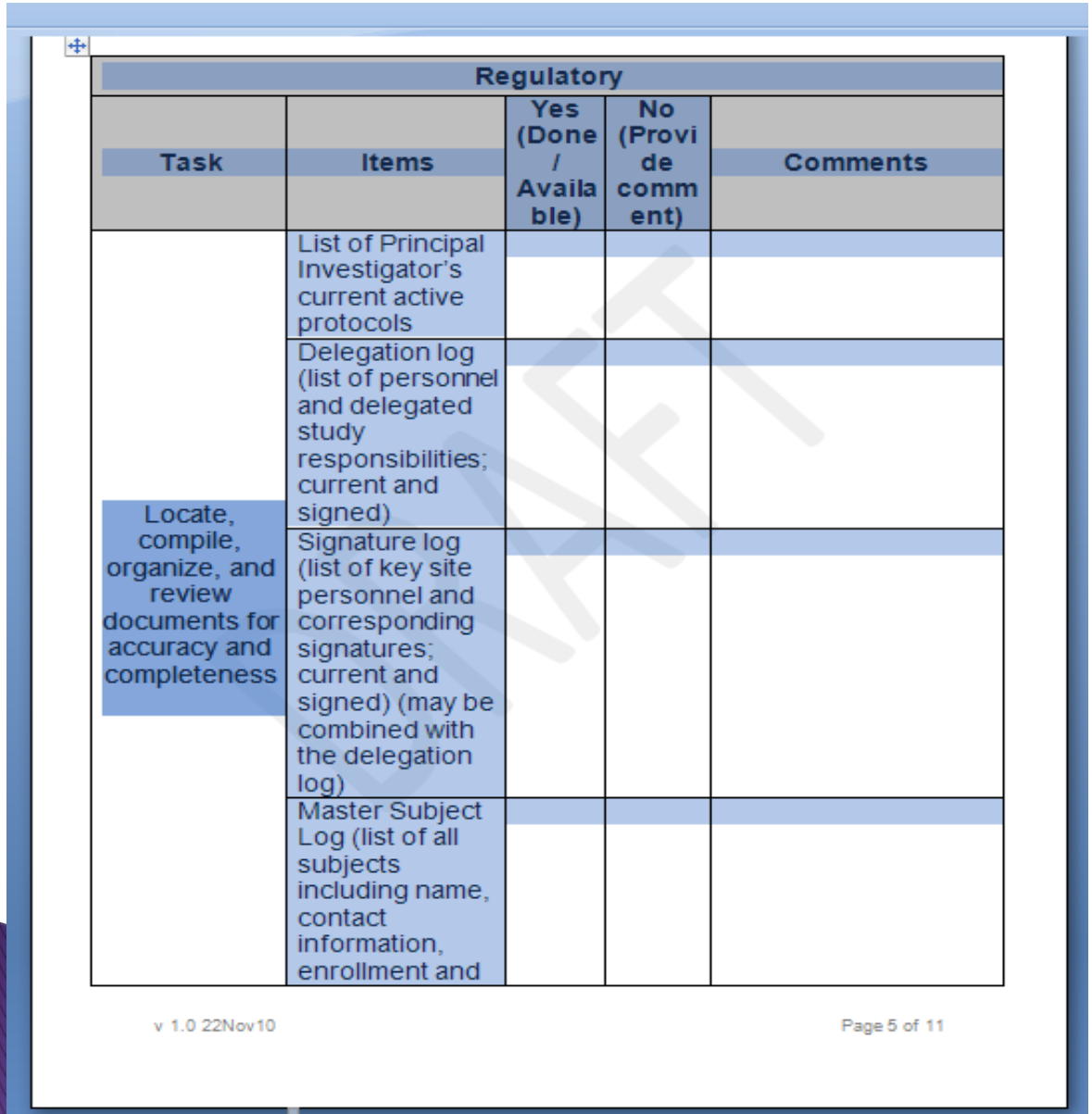
FDA Checklist
Administrative

Site FDA Inspection Preparation Checklist

Administrative				
Task	**Items**	**Yes (Done / Available)**	**No (Provide comment)**	**Comments**
Notify all parties of impending inspection	Sponsor			
	IRB/EC			
	Principal Investigator			
	Sub-Investigator(s)			
	Study Coordinator(s)			
	Pharmacy			
	Laboratory(ies)			
	Medical Records			
	Administration			
	Legal Counsel			
	Reception Area Staff			
	Other (specify in comments)			
Review FDA Inspection Preparation SOP	FDA Inspection Preparation SOP			
Identify work space for the Inspector	Work space			
	Telephone			
	Copier			
	Table			
Review staff and clinic	Review staff schedules			

- Complete later- post FDA training II -2Q013
- Sites will develop SOP

FDA Checklist Regulatory



Regulatory				
Task	Items	Yes (Done / Available)	No (Provide comment)	Comments
Locate, compile, organize, and review documents for accuracy and completeness	List of Principal Investigator's current active protocols			
	Delegation log (list of personnel and delegated study responsibilities; current and signed)			
	Signature log (list of key site personnel and corresponding signatures; current and signed) (may be combined with the delegation log)			
	Master Subject Log (list of all subjects including name, contact information, enrollment and			

- Ensure all documents in place
- Ensure documents are complete, accurate, organized and easily found
- Training Documentation

FDA Checklist
Clinical

Clinical				
Task	Item	Yes (Done/ Available)	No (Provide comment)	Comments
Ensure the following has been completed for each participant	Source documents and medical records are available for each participant (Review for ALCOA)			Alternative: Source documents and corresponding Case Report Forms (CRFs) for each participant are present, clearly identified, and systematically organized in binders or folders for ease of retrieval during the inspection
	Completed Case Report Forms (CRFs) on file for each participant			
	Original signed and dated Informed Consent Forms on file for each participant			
	Inclusion/exclusion criteria for each participant have been met and documented			
	All visits conducted within protocol windows			
	Correct volume of blood and correct tube type drawn at each visit			
	Adverse Events (AEs), and Expedited Adverse Events (EAEs) have been			

v 1.0 22Nov10

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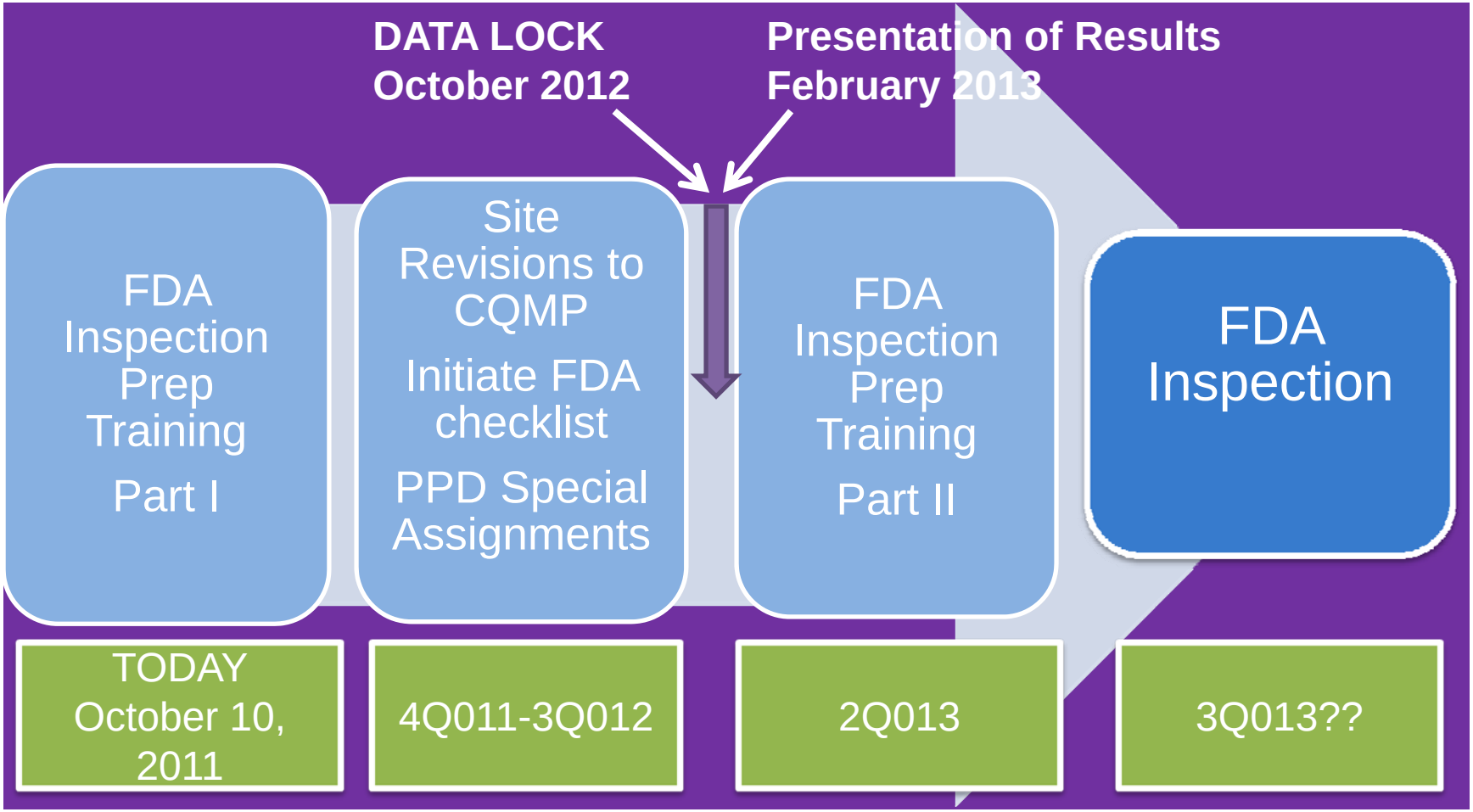
- Determine sample size (OCSO can assist) Recommendation minimum 10% of PIDs per quarter for critical KQIs.

- Customize this checklist as needed

Next Steps

- Access FDA inspection resources on-line
  - Appoint one person to be the “go to “ person and resource for other staff
- Contact your OCSO PO with any questions or concerns

Updated FDA Inspection Preparation Timeline



Remember we're all in this together……

Questions?