Preparing for a United States Food and Drug Administration (FDA) Inspection: VOICE
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
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
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
BIMO conducts on-site inspections of:

- Non-Clinical Laboratories
- Clinical Investigator Sites Principal Investigators
- Institutional Review Boards/Ethics Committees (IRB/EC)
- Sponsors
- Contract Research Organizations (CROs)
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

Clinical Investigator Inspections (CDER, FY 2003-2010)

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)

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*

Overview of the FDA Inspection Process

Three Distinct Phases of an FDA Inspection:

Phase 1  •  Before
Phase 2  •  During
Phase 3  •  After
### FDA Inspection Process

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

Institutional, local, state, and national regulations
# Key Documents

<table>
<thead>
<tr>
<th>Form FDA 1572 – Statement of Investigator</th>
<th>• 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</th>
</tr>
</thead>
<tbody>
<tr>
<td>Form FDA 482 – Notice of Inspection</td>
<td>• FDA written notice of inspection presented by the FDA Inspector at the beginning of the inspection (for US sites only)</td>
</tr>
<tr>
<td>Form FDA 483 – Inspectional Observations</td>
<td>• 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</td>
</tr>
</tbody>
</table>
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
FDA Website

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

- Database of FDA Form 483 Findings
  [http://www.fda.gov/ICECI/EnforcementActions/ucm222557.htm](http://www.fda.gov/ICECI/EnforcementActions/ucm222557.htm)

- Warning Letters
  [http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm](http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm)

- Clinical Trials Section
  [http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm](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
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

802

4225

Monitored
Not monitored

What about the other 84%?
# Monitoring Trends – As of September 14, 2011

<table>
<thead>
<tr>
<th>Monitoring Trends</th>
<th>Findings</th>
<th>Warning Letter Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural Inadequate Source Documentation (A72)</td>
<td>676</td>
<td>Failure to maintain adequate or accurate case histories</td>
</tr>
<tr>
<td>Missed Tests/Study Procedures (A14 [inadeq] = 46, A24 [adeq] = 125)</td>
<td>171</td>
<td>Failure to complete assessments or procedures as required by the protocol&lt;br&gt;Failure to repeat labs as required by the protocol</td>
</tr>
<tr>
<td>Unreported Adverse Events (A62)</td>
<td>23</td>
<td>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</td>
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<tr>
<td>Enrollment Violations (A2)</td>
<td>4</td>
<td>Failure to follow the Inclusion/Exclusion criteria or timelines for enrollment as required by the protocol</td>
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</tbody>
</table>

16%
Site Reported Protocol Deviations – As of September 12, 2011

<table>
<thead>
<tr>
<th>MTN-003 Protocol Deviations</th>
<th>Findings</th>
<th>Warning Letter Examples</th>
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</thead>
<tbody>
<tr>
<td>Omitted Study Procedures</td>
<td>83</td>
<td>Failure to complete assessments or procedures as required by the protocol</td>
</tr>
<tr>
<td>Missed Repeat Labs</td>
<td>32</td>
<td>Failure to complete assessments or procedures as required by the protocol</td>
</tr>
<tr>
<td>Study Product Errors – Study Product Hold (17) Study Product Dispensing (14)</td>
<td>31</td>
<td>Failure to adequately document study drug accountability or failure to hold the study drug as required by the protocol</td>
</tr>
<tr>
<td>Enrollment Deviations</td>
<td>26</td>
<td>Failure to follow the Inclusion/Exclusion criteria or timelines for enrollment as required by the protocol</td>
</tr>
</tbody>
</table>
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.
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
Informed Consent
Eligibility
ICH GCP/GLP
Sponsor Requirements
Ethical Principles
Laws and Regulations
Informed Consent

Eligibility

Study Procedures

Study Product Management

Clinical Management

Laboratory Evaluations

Data Management

Regulatory Management

Informed Consent

Ethical Principles

Laws and Regulations

ICH GCP/GLP

Sponsor Requirements

NIAID/DAIDS

CORE FHI

SCHARP SDMC

Network Laboratory

IRB/EC

PPD CSSM
Quality Management Plan(s)

Ethical Principles
Laws and Regulations
ICH GCP/GLP
Sponsor Requirements

Data Management
Regulatory Management
Informed Consent
Eligibility
Laboratory Evaluations
Clinical Management
Study Procedures
Study Product Management

Quality Management

NIAID/DAIDS
MTN/CORE FHI
SCHARP SDMC
Network Laboratory
IRB/EC
PPD CSSM

FDA Inspection Preparedness
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

FDA Inspection Preparedness
Objective Check

- Describe the relationship between quality management activities and FDA inspection preparedness
Roles and Responsibilities
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
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
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
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)](http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/qmppolicy.pdf)
Quality Control

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?

Sample Size 100%

Frequency Real-time, daily
What will be reviewed? Consider Key Quality Indicators.

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

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

How will errors be corrected?

How will errors be documented for analysis?

How will the errors, corrective actions, and preventive actions be communicated?
Internal Quality Management Reporting Structure

- Quality Control Log
- Quality Assurance Tools
- Summary Report
- Annual Summary Report
- Data Gathering
- Communication
### MTN-003 Study Implementation Materials

#### Visit Checklists

<table>
<thead>
<tr>
<th>Visit Description</th>
<th>Date</th>
<th>File Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01: Screening, Part 1</td>
<td>2010-Apr-16</td>
<td>97.5 KB</td>
</tr>
<tr>
<td>02: Between Screening Part 1 and Screening Part 2 Worksheet</td>
<td>2010-Apr-16</td>
<td>63 KB</td>
</tr>
<tr>
<td>03: Screening, Part 2</td>
<td>2010-Apr-16</td>
<td>89.5 KB</td>
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<td>04: Screening, Pelvic Exam</td>
<td>2010-Apr-16</td>
<td>70.5 KB</td>
</tr>
<tr>
<td>05: Between Screening Part 2 and Enrollment Worksheet</td>
<td>2010-Apr-16</td>
<td>67.5 KB</td>
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<tr>
<td>06: Enrollment</td>
<td>2010-Apr-16</td>
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<td>07: Month 1 Visit</td>
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<td>08: Monthly Visit</td>
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<td>09: Quarterly Visit</td>
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<td>11: Semi Annual Visit</td>
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<td>12: Annual Visit</td>
<td>2010-Apr-16</td>
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<tr>
<td>13: Product Use End Visit (PUEV)</td>
<td>2010-Apr-16</td>
<td>107 KB</td>
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<tr>
<td>14: Termination/Study Exit Visit</td>
<td>2010-Apr-16</td>
<td>98 KB</td>
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<tr>
<td>15: Interim Visit Checklists</td>
<td>2010-Aug-16</td>
<td>75.5 KB</td>
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<tr>
<td>16: HIV Sample 2 Visit Checklist</td>
<td>2010-Aug-16</td>
<td>43.5 KB</td>
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<tr>
<td>17: Post-Seroconversion Checklist</td>
<td>2011-Mar-21</td>
<td>57.21 KB</td>
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</table>
Quality Assurance Tools

SCHARP QC Reports

MTN CORE-FHI Assessment Reports

PPD Monitoring Reports

Quality Control Tools

SCHARP DM Quality Report

Communicate

Quality Management Summary Report Tool

Trending
Objective Check

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

<table>
<thead>
<tr>
<th>Monitor (3)</th>
<th>Quality Control (10)</th>
<th>Quality Assurance (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>555100117</td>
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<td>555100115</td>
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</tbody>
</table>
Problems and Trends Found

Now What?
Problem-Solving Model

1. Define Problem
2. Analyze Data
3. Identify Solutions
4. Select Best Solution
5. Develop Action Plan
6. Implement Solution
7. Evaluate Solution

Root Cause Analysis
Define Problem

Problem-Solving Model

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

Problem-Solving Model

Define Problem

Analyze Data

Root Cause Analysis

Identify Solutions

Select Best Solution

Develop Action Plan

Implement Solution

Evaluate Solution

Analyze Data
Identify Solutions

Problem-Solving Model

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

Select Best Solution

Define Problem

Analyze Data

Identify Solutions

Root Cause Analysis

Evaluate Solution

Implement Solution

Develop Action Plan

Select Best Solution
Develop Action Plan

Problem-Solving Model

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

Problem-Solving Model

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

Problem-Solving Model

- Define Problem
- Analyze Data
- Identify Solutions
- Select Best Solution
- Develop Action Plan
- Implement Solution
- Evaluate Solution

Root Cause Analysis
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
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

<table>
<thead>
<tr>
<th>Task</th>
<th>Items</th>
<th>Yes (Done / Available)</th>
<th>No (Provide comment)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notify all parties of impending inspection</td>
<td>Sponsor</td>
<td></td>
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<td></td>
<td>IRB/EC</td>
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<tr>
<td></td>
<td>Principal Investigator</td>
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<td>Sub-Investigator(s)</td>
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<td>Study Coordinator(s)</td>
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<td></td>
<td>Pharmacy</td>
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<td>Other (specify in comments)</td>
<td></td>
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</tr>
<tr>
<td>Review FDA Inspection Preparation SOP</td>
<td>FDA Inspection Preparation SOP</td>
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<tr>
<td>Identify workspace for the Inspector</td>
<td>Work space</td>
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<td></td>
<td>Telephone</td>
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<td>Table</td>
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<tr>
<td>Review staff and clinic</td>
<td>Review staff schedules</td>
<td></td>
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</tr>
</tbody>
</table>

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

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

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

<table>
<thead>
<tr>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source documents and medical records are available for each participant (Review for ALCOA)</td>
</tr>
<tr>
<td>Completed Case Report Forms (CRFs) on file for each participant</td>
</tr>
<tr>
<td>Original signed and dated Informed Consent Forms on file for each participant</td>
</tr>
<tr>
<td>Inclusion/exclusion criteria for each participant have been met and documented</td>
</tr>
<tr>
<td>All visits conducted within protocol windows</td>
</tr>
<tr>
<td>Correct volume of blood and correct tube type drawn at each visit</td>
</tr>
<tr>
<td>Adverse Events (AEs), and Expedited Adverse Events (EAEs) have been reported</td>
</tr>
</tbody>
</table>

- 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
Remember we’re all in this together............
Questions?