Agenda

- External audits
- Best practices to get ready for audits
External Audits

- Food and Drug Administration
- Office of Human Research Protections
- Office of Inspector General
What to do when the FDA calls to schedule a site visit …

Obtain the following information:
- Call date
- Starting date of audit and expected duration
- Name of the person making the call
- Telephone number for questions
- FDA Investigator contact information/Title
- Additional FDA Investigators names?
Ask Questions

- **Who / what is being inspected?** Wait for specific answers. Do not make suggestions.
- **Which clinical trial/study?**
- **Principal Investigator/Co-Investigator(s)?**
- **Other details?**
- **Why is the inspection being done?** Wait for the answer. Do not make suggestions.
- **Routine (i.e. IND)?**
- **Directed (for cause)?**
- **Follow-up (i.e. 483; warning letter)?**
Other Details?

Does the FDA want specific personnel available?
  – If yes, then list

Who/When?

Does the FDA want specific documents available?
  – If yes, then list

Does the FDA want any of these documents sent prior to their arrival?
  – How? Send to overnight registered address? Use certified mail.
  – Delivery by when?
What should I do first?

Please immediately send notification to the following individuals in the Duke University Ethics and Compliance Office:

- Tina Tyson, JD, Chief Ethics and Compliance Officer
  Tina.tyson@duke.edu / 684-2475

- Margaret Groves, JD, CRA, CCRP, Director CTQA
  Margaret.groves@duke.edu / 684-3133
General Preparation

- Notify parties involved with your study
  - Sponsor (if required)
  - Study team
  - CRU
  - IRB
  - University Counsel’s Office
  - Pharmacy (if applicable)
  - Laboratories (if applicable)
  - Medical Records (if applicable)
General Preparation (cont’d)

- Respond in an appropriate and timely fashion
- Request necessary medical records and/or electronic case report form access
- Reserve workspace for reviewer/auditor
- Arrange for a large table, as well as phone and copier access
Organize Files

Regulatory
- Protocol (all versions)
- Investigator Brochure (all versions)
- Protocol Amendments
- FDA Form 1571/1572 (all versions)
- Investigator Agreements
- CVs for PI and Staff
- Medical Licenses
- IND/IDE Documents
- Enrollment/Screening Logs
- Delegation of Authority Log
- Drug Package Insert (if applicable)
Organize Files (cont’d)

**IRB Files**
- Approval Letter for Initial Protocol with Original Consent Form
- All Continuing Review Approval Letters and Original Updated Consent Forms
- All Amendment Approvals
- All Versions of Consent Documents for Screened and Enrolled Subjects
- All Status/Progress Reports for:
  - IRB Approved Renewal(s)
  - Adverse Events
  - Deaths
  - Study Termination
  - Final Summary
Organize Files (cont’d)

- Correspondence and Phone Logs
  - All Sponsor Correspondence
  - All CRO Correspondence (if applicable)
  - All FDA Correspondence
  - All IRB Correspondence
  - Monitoring and Auditing Logs
Organize Files (cont’d)

- Laboratory
  - Laboratory Certification and Normal Ranges
  - Up to Date CV of Laboratory Director

- Research Test Article Accountability
  - Receipt Log
  - Dispensing Log
  - Return and Destruction Log
  - Storage Temperature Log
Organize Files (cont’d)

Subject Documentation
- Complete Case Report Forms for Each Subject Enrolled
- Complete Source Documents for Each Subject Enrolled
- Verification of Inclusion/Exclusion Criteria
- Contact DOCR to Request Limited Access to eBrowser and MaestroCare for FDA
Day of the Review

- Have the following personnel available to the auditor:
  - Routine Audit:
    - Study Staff
  - For Cause Audit
    - Study Staff
    - Ethics and Compliance Office Representative
- Ask to see 482 Notice of Inspection and auditor’s credentials
On-Site Conduct

Responding to FDA:

- Be concise, direct, and truthful
- Answer only questions asked, do not volunteer information
- Ask for clarification if you do not understand a question
- If you don’t know an answer, say so, don’t guess
- Tell the auditor if you later realize you gave incorrect information

Ensure that all staff are educated on proper conduct during an FDA Inspection.
On-Site Conduct (cont’d)

- Be available to answer questions or arrange logistics if interviews are requested
- Take notes on questions auditor asks
- Make duplicate copies of all documents that auditor requests to be copied
- Routine Audit: Provide daily reports to study team and CRU
- For Cause Audit: add IRB leadership, Vice Dean for Research, Chief Compliance Officer, Associate Dean for Clinical Research and Associate Dean for Research Support Services to daily report distribution
FDA Audit Plan

Review of Each Subject Enrolled or Possibly Only Those Chosen for Review

- Are case report forms complete for each subject?
- Are data collection forms complete?
- Is inclusion/exclusion criteria documented?
FDA Audit Plan (cont’d)

Review of Source Documentation for Each Subject Enrolled that Documents the Following:

- Condition of the Subject at the Time of Entry (Inclusion/Exclusion Criteria)
- Exposure to Research Article
- Concomitant Medications
- Clinical Assessments of the Subject During the Study
- Laboratory Reports
- Diagnostic Tests
- Dose Modification
- Adverse Events/Deaths
- Protocol Exemptions
- Early Termination
FDA Audit Plan (cont’d)

- Review of Files/Logs
  - Regulatory
  - IRB
  - Correspondence and Phone Logs
  - Laboratory
  - Research Test Article
FDA Audit Plan (cont’d)

At the conclusion of the on-site review, there will be an Exit Meeting:

– Typical Findings
  - No Actions Indicated
  - Voluntary Actions Indicated
  - FDA 483 Inspectional Observations

If you receive a 483, please call Duke Ethics and Compliance Office immediately so that we can assist you with your responses!
Ethics and Compliance Office
Advisory Role

Not Just about Human Subject/Billing Reviews, Research Financial Compliance or Other Risk Areas

- A Source of Information and Guidance on Compliance Areas
- Prevention of Future Compliance Problems through Education
- Educational Compliance Reviews
- University Compliance monitoring
Reporting Compliance Concerns

Contact the Ethics and Compliance Office:

- Duke Medicine Integrity Line: 1-800-826-8109
- Duke University Compliance and Fraud Hotline 1-800-849-9793
  - Compliance concerns can be reported anonymously
  - Non-retaliation and non-retribution policy
- MCAdmin Clinical Trials Quality Assurance
  clinica4@dm.duke.edu
  http://medschool.duke.edu/research/compliance-office
  http://duke.edu/services/ethicscompliance
Compliance Office Contact Information

Tina R. Tyson, JD, Chief Ethics and Compliance Officer, tina.tyson@duke.edu

**CTQA and Billing Compliance**, clinica4@dm.duke.edu
Margaret Groves, Director, margaret.groves@duke.edu
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Malissa Harris, Senior Compliance Auditor, malissa.harris@dm.duke.edu
Vivian Jordan, Compliance Auditor, vivian.jordan@duke.edu
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**Ethics & Compliance Monitoring**
Ericka Kranitz, Director, ericka.kranitz@duke.edu
Liddy Staker, Senior Compliance Auditor, liddy.staker@dm.duke.edu
Questions?