| Wake Forest Baptist Medical Center | **External Audits of Human Subjects Research**<br>RARI-S-03-05 | **Dept:** | **CTSI** |
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| | | **SOP Number:** | 05 |
| | | **Effective Date:** | 10/18/17 |
| | | **Current (Revised) Date:** | |
| | | **Contact:** | **Office of Regulatory Affairs and Research Integrity - CTSI** |
| **Approval Signature:** | | **Date of Signature:** | 10/18/17 |
| **Name and Title:** Christopher O'Byrne VP, Research Admin + Operations | | | |

1) **General Procedure Statement:**
It is the standard operating procedure (SOP) of Wake Forest Baptist Medical Center to comply with all regulatory requirements related to audits of human research by federal oversight officials. This includes the Office of Human Research Protections (OHRP) when the study falls under the regulations found at 45 CFR 46, and the Food and drug Administration (FDA) if the study falls under the regulations found at 21 CFR 50. In addition, it is our standard to comply with audits conducted by federal funding agencies of studies subject to audit by a federal funder.

   a) Scope: This policy applies to faculty, staff, students, and other individuals engaged in research activities under the oversight of WFBMC regardless of funding source.

   b) Responsible Department/Party/Parties:
      i. Procedure Owner: Clinical Translational Science Institute (CTSI)
      ii. Procedure: Office of Regulatory Affairs and Research Integrity
      iii. Supervision: Office of Regulatory Affairs and Research Integrity
      iv. Implementation: Office of Regulatory Affairs and Research Integrity

2) **Definitions:** For purposes of this SOP, the following terms and definitions apply:

   a) **WFBMC:** Wake Forest Baptist Medical Center and all affiliated organizations including Wake Forest University Health Sciences (WFUHS), North Carolina Baptist Hospital (NCBH), all on-site subsidiaries as well as those off-site governed by WFBMC policies and procedures.
   b) **Research:** Means a systematic investigation designed to develop or contribute to knowledge and may include the stages of development, testing, and evaluation.
   c) **Research Data:** Means all information in whatever form (e.g. both physical and electronic). For the purposes of this policy, Research Data are further defined as including any records that would be used for **the** reconstruction and evaluation of reported or otherwise published results. Research Data also includes materials such as unmodified biological specimens and environmental samples. Research Data differ among disciplines. Examples of Research Data and Materials include laboratory and other notebooks, notes of any type, photographs, films, digital images, original biological and environmental samples, protocols, numbers, graphs, charts, numerical raw experimental results, instrumental outputs from which Research Data can be derived, case report forms, patient charts, and other source documentation for human research studies.
   d) **Clinical Trial** – The NIH defines a clinical trial as a prospective biomedical or behavioral research study of human subjects that is designed to determine the safety, efficacy, and effectiveness of biomedical (drugs, nutritional supplements, surgical intervention, or devices) or

behavioral (diet, physical activity, cognitive therapy, etc.) interventions.

e) **Research Records**: Information recorded for the purpose of a research study, regardless of form or the media on which it may be recorded. Research records include the Case Report Form, Regulatory Binder, Consent Form and Source Data.

f) **Case Report Form (CRF)** – Document (printed or electronic) designed to record all of the protocol required information to be reported to the sponsor on each trial subject. (ICH GCP 1.11)

g) **Informed Consent Forms (ICF)** – Documents that provide a description of the study and are signed by both the study participant and a member of the study team.

h) **Adverse Event (AE)** – Any untoward or unfavorable medical occurrence in a clinical research study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

i) **Enrolled Subject**- The WFUHS IRB considers any subject who signs a consent form to be an enrolled subject, even if they are subsequently found not to qualify for the study.

j) **Regulatory Binder (or Files)** – Place where all study-specific information and regulatory documentation, including IRB approved protocols, amendments, informed consent, case report forms, FDA 1571 and 1572 (if applicable) and recruitment materials, is maintained. The regulatory binder provides a thorough history of the research study from protocol development to study completion.

k) **Source Data** – Information contained within source documents that represent the original documentation of findings and observations of subjects participating in clinical research studies (ICH GCP 1.51).

l) **Source Documents** – Original documents, data and records such as medical records, laboratory results, x-rays, pharmacy records and subject diaries. (ICH GCP 1.52).

**3) Procedure Guidelines:**

**Preparation for an Inspection**

**I. Upon notification from a federal funding agency, OHRP or the FDA to schedule an inspection:**

1. Obtain the following information:
   a. Lead inspector name and contact information
   b. Name of studies or PI (for OHRP and FDA) being inspected
   c. Starting date and expected duration
   e. Reason for the inspection (most will be "routine")
   f. Requests for specific personnel and documents

2. Notify WFUHS Compliance Office, the IRB, and the Legal Department immediately if:
   a. The reason for the inspection is "directed" (i.e., for cause), or
   b. An FDA investigator arrives at your site unannounced.

**II. Before the site inspection:**

1. Notify the following parties who may be involved, including, but not limited to:
   a. All study staff (PI, Co-Inv., Research Coordinator, etc.)
   b. Sponsor (If applicable)
   c. IRB
   d. Monitoring and Oversight
   e. Investigational Drug Service (if applicable)

2. Talk with the representative from Oversight and Outreach (O&O) and:
   a. Arrange a meeting to review the inspection process
   b. Request that O&O conduct a pre-inspection review of your study documents

3. Prepare an overview of the study to be kept as a reference for the PI and study staff. Include:
   a. Summary of the study
   b. Enrollment #s
   c. Adverse events
   d. SAEs/Deaths
   e. Deviations
   f. Any other information (e.g. exceptions to inclusion/exclusion criteria) that may be helpful

4. For FDA audits prepare a list of all clinical trials for which the PI has been responsible; include title, start, and stop date. If the list would be excessive, limit it to those trials that were open throughout the duration of the study(ies) under inspection.

5. Identify a person who will serve as the general contact person for the inspector. This person will serve as an escort, will oversee the inspection, and will need to be readily available to the inspector at all times.
6. Make sure all medical records are readily available. Request electronic access to the medical records by completing the "WakeOne Access for Monitors Form." Be sure to note that the monitor is a federal inspector.

7. Reserve a room in a private area for the inspection. Records or study materials from other studies should not be present in this room. Make sure that there is a copy machine located close to the room.

8. Review identified records to:
   a. Ensure comprehensiveness, accuracy and compliance
   b. Identify weakness/gaps
   c. Correct items that that can be corrected using appropriate correction methods (i.e. draft notes-to-file, locate missing documents, never use white-out, and always retain originals.)
   d. Identify any items noted during prior audits or monitoring visits and ensure that those items have been appropriately handled and processes put in place to prevent reoccurrence.
   e. Develop and implement corrective action plan to address any identified problems.

9. Ensure that all study documents (consent forms, CRFs, supporting source documents, regulatory documents, enrollment/screening logs, and sponsor correspondence) are available for review by the inspector. Standard procedure is for the inspector to request files for review, starting with the "general" study materials including the regulatory documents binders, then all signed informed consent forms, followed by a sampling of specific patient records. Study finances and personnel records are not included in the standard inspection.

10. Identify and have copies available of all IRB correspondence (e.g., approvals, continuing reviews, current consent, etc.). These documents should be readily available for review by the inspector, if the inspector requests them. If some documents are missing, contact the IRB to obtain an additional copy.

11. Track and document preparation activities; an Audit Preparation Checklist is available on the MO website under "checklists"

**III. Actions to be taken during the site inspection:**

1. Designate a person to oversee the inspection. The person, usually the research coordinator, should be knowledgeable about the study activities and records, and be able to coordinate with the study PI and other study personnel.

2. The Principal Investigator (PI) or his/her designee should be available when the inspector first arrives. Request to see the inspector's identification, if he/she does not present it to you. For FDA inspections, write down the inspector's badge number. Ask to see his/her credentials at the beginning of each day, or until the inspector advises you to do otherwise.

3. For FDA inspections, the inspector will present a Notice of Inspection (Form FDA 482) to the PI for a signature. The presentation of this Notice officially authorizes and begins the inspection.

4. The inspector may request a tour of the facility areas where the research took place. The escort should accompany the inspector at all times.

5. The inspector may ask the PI for a list of the PI's other studies and request the PI to summarize and discuss the study identified for the inspection.

6. The inspector will request files for review. Provide the inspector only with files that have been requested. Do NOT volunteer information.

7. The inspector will request copies of some documents. Remove subject identifiers from the copies given to the inspector. Make a copy for yourself of any documents that are requested. The inspector's copies should be stamped "Confidential" and your copies should be stamped "Copy."

8. The PI should set aside time each day to talk with the inspector, as well as being available for questions that may arise.

9. Responses to the inspector's questions:
   a. Answer all questions honestly and completely
   b. Listen carefully and only answer what was asked
   c. Be concise and clear with the answers
   d. Keep a log of questions asked by the inspector
   e. DO NOT volunteer information
   f. DO NOT guess or speculate. If you don't know the answer, do not be afraid to tell the inspector this. Defer to other study staff if you believe that they might know the answer to the question.
   g. DO NOT lie, argue, or panic
   h. DO NOT sign affidavits. If the FDA presents an affidavit for signature, tell the inspector that you must consult with the University's legal counsel before signing any affidavit and then immediately contact the Medical Center Compliance Office for guidance.

10. During the inspection, the person overseeing the inspection should coordinate all requests and take notes to be written up at the conclusion of the inspection.

**IV Actions to be taken after the site inspection:**

1. Exit Interview: The inspector will usually hold an exit interview at the conclusion of the inspection. The escort, Principal Investigator, and any other appropriate staff should attend this interview.

2. During the exit interview:
   a. The escort should document the conversation, noting observations, comments, and commitments

b. The inspector will review the findings and note any deficiencies. For FDA inspections these any deficiencies will be noted on the Inspectional Observations Form FDA 483. If no deficiencies are found or the inspector has comments that he/she believes are not serious enough to warrant a Form FDA 483, then no form will be issued.

**4) Review/Revision/Implementation**

a) Review Cycle: This SOP shall be reviewed by the Office of Regulatory Affairs and Research Integrity at least every three years from the effective date.

b) Office of Record: After authorization, the Legal Department shall house this SOP in a policy database and shall be the office of record for this SOP.

**5) Related Policies and SOPs**

Policy on the Quality Conduct of Research
HRPP Standard Operating Procedures

**6) Governing Law or Regulations**

Title 45 Code of Federal Regulations Part 46
Title 21 Code of Federal Regulations Part 50
Title 21 Code of Federal Regulations Part 312
Title 45 Code of Federal Regulations Part 164

**7) Attachments**

None

**8) Revision Dates**

July 25, 2017