Wake Forest Baptist Medical Center	**Internal Post-approval Monitoring of Human Subjects Research** RARI-S-03-03	**Dept:**	**CTSI**
		SOP Number:	03
		Effective Date:	10/18/17
		Current (Revised) Date:	
		Contact:	**Office of Regulatory Affairs and Research Integrity - CTSI**
Approval Signature:		**Date of Signature:**	10/15/17
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 conduct routine post-approval monitoring of selected human research studies. The Human Research Oversight and Outreach team within the Office of Regulatory Affairs and Research Integrity carries out these monitoring visits. The purpose of the Oversight & Outreach Program (O&O) is to improve the quality of the human subjects' protection program through education, training, and post approval monitoring of research studies. This program is intended to be proactive, not punitive, and focuses on educating investigators and research staff about their ethical and regulatory responsibilities in the conduct of research. The monitoring visits help investigators ensure that human research meets the regulatory requirements set forth in the regulations found at 45 CFR 46, 21 CFR 50, 45 CFR 164, Institutional Review Board (IRB) SOPs, and other laws, regulations, and Medical Center policies as applicable. In addition, monitoring may be performed as part of a corrective action plan directed by the IRB, or as requested by the study team in preparation for an external audit.

   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:

Selection of studies for monitoring visits:

A "Random" review is conducted as a normal part of the Oversight & Outreach program to ensure that the safety, rights and welfare of research subjects are properly protected and to identify any educational and/or training needs the study team might have as related to the research. Protocols are selected for a review by performing a query of the IRB database. Any study that has WFUHS IRB approval may be reviewed. This type of review includes, but is not limited to, all research records and documents, observations of processes, and interviews with research team members.

Monitoring directed by the IRB as a part of corrective action is usually focused on ensuring that a particular study meets the requirements of the corrective action plan and any other applicable regulatory and policy requirements. The O&O team can assist the investigator with training or procedural suggestions to help ensure the study team is well equipped to comply with IRB requirements.

Study teams are encouraged to request assistance from O&O when preparing for an external audit. This is helpful in making sure that study records are complete and properly organized for inspection.

The following items should be available for review by O&O:

- The regulatory binder
- All signed consent forms
- Source documentation and research records for all enrolled subjects.

Time Required for Review:

The length of time a review will take depends on:

- The complexity of the study
- The number of subjects enrolled
- The length of time the study has been active
- The organization of the research records and regulatory files

The number of records reviewed depends on the type of review (random vs. for cause) and the number of subjects enrolled. Generally, in a random monitoring visit all signed consent forms are reviewed along with a random sampling of 10% of the research records/source documents. All study records should be kept in a manner that allows for easy retrieval and review. If deficiencies are identified, then additional research records may be reviewed.

Notification of an upcoming monitoring visit:

The Principal Investigator is notified electronically via e-mail or in writing that a particular study has been selected for a review. (Note: Individuals listed as study team members in e-IRB may also be copied on the notification.) The study team and Oversight & Outreach will arrange a date/time for the review, typically within 2-4 weeks of notification.

During the Review:

An introductory discussion is held at the beginning of the visit so that O & O has a clear picture of how the study is being conducted. The responsibilities and roles of the staff members are discussed. The objectives of the monitor's visit will be discussed and timelines will be established for intermittent meetings and follow-up during and after the review.

A tour of the facility will be performed to examine the equipment being used and their location (i.e. - calibration logs and maintenance logs). Storage areas for case report forms and test articles will be examined for accessibility and security.

A sample of subject data will be selected to verify protocol compliance, source documentation, and case report form completion. Verification of administration and signing of the study consent form will be completed for all (or a subset) research subjects.

A review and observation of study staff work practices will be performed. Examples of this would be 1) a review of the standard operation procedures for conducting clinical research, 2) the process in which the informed consent is administered, 3) the recruitment process, 4) reporting of serious adverse events, 5) drug accountability and the process for which randomization blind may be broken.

A Closing (Exit) Meeting will be conducted at the end of the scheduled monitoring and oversight review.

All significant findings and follow-up items will be discussed. The study staff will be able to respond to the findings and note any corrective action already taken during the review.

Monitoring Report:
A copy of the Oversight & Outreach report is shared with the Assistant Dean for Regulatory Affairs & Research Integrity, the IRB Director, and the IRB Executive Chair. A follow-up letter is sent to the Principal Investigator and Study Coordinator outlining all findings as well as any corrective actions required by the study team. The investigator should provide a written response to the follow-up letter within 30 days documenting the corrective actions taken and study revisions made in order to eliminate future recurrences of any problems.

In cases where major deficiencies are identified, a meeting with the Principal Investigator, study coordinator, IRB Director, IRB Executive Chair, and Oversight & Outreach may be scheduled to clarify discrepancies/deficiencies and to develop a corrective action plan to prevent further recurrences.

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