Wake Forest Baptist Medical Center	**Standard Operating Procedure on the Registration of Clinical Trials in clinicaltrials.gov** RARI-S-03-06	**Type:**	**Tier 3**
		Original Effective Date:	10/20/2017
		Current (Revised) Date:	
		Contact:	Office of Regulatory Affairs and Research Integrity - CTSI
Approval Signature:		**Date of Signature:**	10/20/17
Name and Title: Christopher O'Byrne VP, Research Admin + Operations			

1) **General Policy Statement:**
   It is the policy of Wake Forest Baptist Medical Center to comply with Federal regulations
   a) Scope: This standard operating procedure (SOP) applies to faculty, staff, students, and other affiliated individuals engaged in human research activities.
   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) **FDAAA Final Rule –** This final rule details the requirements for submitting registration and summary results information, including adverse event information, for specified clinical trials of drug products (including biological products) and device products and for pediatric post-market surveillances of a device product to *ClinicalTrials.gov*, the clinical trial registry and results data bank operated by the National Library of Medicine (NLM) of the National Institutes of Health (NIH). This rule provides for the expanded registry and results data bank specified in Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) to help patients find trials for which they might be eligible, enhance the design of clinical trials and prevent duplication of unsuccessful or unsafe trials, improve the evidence base that informs clinical care, increase the efficiency of drug and device development processes, improve clinical research practice, and build public trust in clinical research. The requirements apply to the responsible party (meaning the sponsor or designated principal investigator) for certain clinical trials of drug products (including biological products) and device products that are regulated by the Food and Drug Administration (FDA) and for pediatric post-market surveillances of a device product that are ordered by FDA.
   c) **NIH ClinicalTrials.gov Policy –** The National Institutes of Health Policy on Clinical Trials Registration applies to both the public and private sectors. Its purpose is to inform future research and research funding decisions, mitigate bias (e.g., non-publication of results, especially negative results), prevent duplication of unsafe trials, meet ethical obligation to human subjects (i.e., that results inform science), and increase access to data about marketed products.
   d) **ICMJE Policy** - Briefly, the International Committee of Medical Journal Editors (ICMJE) requires, and recommends that all medical journal editors require, registration of clinical trials in a public trials registry at or before the time of first patient enrollment as a condition of consideration for publication. Editors requesting inclusion of their journal on the ICMJE website

list of publications that follow ICMJE guidance should recognize that the listing implies enforcement by the journal of ICMJE's trial registration policy.

e) **Responsible party** – The entity responsible for registering the trial is the "responsible party." The statute defines the responsible party as: (1) the sponsor of the clinical trial (as defined in 21 C.F.R. 50.3), or (2) the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee (provided that "the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements" for submitting information under the law.)

f) **Applicable Clinical Trial as defined by FDAAA** – Applicable clinical trials are (1) clinical trials of drug and biological products that are controlled, clinical investigations, other than phase 1 investigations, of a product subject to FDA regulation; and (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies) or any pediatric post-market surveillance studies required by FDA under the FD&C Act. ► *All applicable clinical trials must be registered in clinicaltrials.gov and results must be submitted.*

g) **Clinical Trial as defined by the NIH** – A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. ► *Registration and results submission to ClinicalTrials.gov of all NIH-funded clinical trials is required, regardless of phase or type of intervention.*

h) **Clinical Trial as defined by ICMJE** - In June 2007 the ICMJE adopted the WHO's definition of clinical trial: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes." Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example, drugs, surgical procedures, devices, behavioral treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. The ICMJE member journals implemented the expanded definition of clinically directive trials for all trials that began enrollment on or after July 1, 2008.

1) **Policy Guidelines:**

a) For the purpose of this SOP Wake Forest Health Sciences will be considered the responsible party for all investigator initiated clinical trials requiring registration under federal policy or any other investigator initiated clinical trial that the investigator wishes to voluntarily register. However, it is the responsibility of the Principal Investigator to register the study and maintain that record in compliance with regulatory requirements, in clinicaltrials.gov.

b) A centralized support, ClinicalTrials.gov administrator, in the Clinical and Translational Science Institute (CTSI) is available to assist with instruction on registration, updating trial records, resolving record problems and reporting results. Principal Investigators may request assistance from the ClinicalTrials.gov administrator or the administrator may contact the investigator to provide instruction if the ClinicalTrials.gov record is out of compliance with regulatory requirements. In instances when an investigator is contacted by the ClinicalTrials.gov administrator because a record is out of compliance, s/he is expected to provide the ClinicalTrials.gov administrator with the information necessary to restore the record to compliance in a timely and accurate manner. Principal Investigators may communicate this

information to the CTSI administrator by telephone, email or via entering information into the WISER system.

c) Compliance with the FDAAA Final Rule, NIH Policy, and to protect the ability to publish results per the ICMJE, requires adherence to the following timelines.

Registration

- **FDAAA** - Not later than 21 days after enrollment of the first participant.
- **NIH supported Study** - Not later than 21 days after enrollment of the first participant.
- **ICJME** – Prior to enrollment of first participant.

To register a study, fill out all of the required fields as specified by ClinicalTrials.gov. Once completed, the record will be reviewed by a member of the CTSI regulatory team for release. Your registration will be complete once the record is public, the NCT number has been received, and all FDAA and ICJME elements have been completed.

Updates

- **FDAAA** - For clinical trials initiated before the effective date of the final rule, § 11.64(a)(1)(i)(A) establishes a general requirement for responsible parties to update clinical trial registration information specified in section 402(j)(2)(A)(ii) **not less than once every 12 months** if there are changes to any of the data elements previously submitted.
- Section 11.64(a)(1)(i)(B) and (a)(1)(i)(C) detail the requirement to update the **Overall Recruitment Status** data element not later than 30 calendar days after any change in overall recruitment status and the **Primary Completion Date** data element not later than 30 calendar days after the clinical trial reaches its actual primary completion date.

For clinical trials initiated on or after the effective date of the final rule, § 11.64(a)(1)(ii)(A) establishes a general requirement for responsible parties to update clinical trial registration information specified in § 11.28 not less than once every 12 months if there are changes to any of the data elements previously submitted. Changes to certain data elements must be updated more rapidly than once every 12 months.

- Section 11.64(a)(1)(ii) outlines the requirements for updating the following 14 data elements:
  (a) The **Study Start Date** data element must be updated from estimated to actual not later than 30 calendar days after the first human subject is enrolled in the clinical trial.
  (b) The **Intervention Name**(s) data element must be updated to a non-proprietary name not later than 30 calendar days after a non-proprietary name is established for an intervention studied in a clinical trial. Intervention Name is frequently used as a search term to identify and retrieve clinical trials of interest.
  (c) Clinical trial information submitted under the **Availability of Expanded Access** data element in § 11.28(a)(2)(ii)(H) must be updated by the responsible party who is both the manufacturer of the drug and the sponsor of the applicable clinical trial not later than 30 calendar days after expanded access becomes available. Similarly, the data element must be updated not later than 30 calendar days after the date on which the

responsible party receives an NCT number for the expanded access record.

(d) The **Expanded Access Status** data element in § 11.28(c)(2)(iv) must be updated not later than 30 calendar days after a change in the status of the availability of expanded access, to indicate whether access to the investigational drug product is currently available. This data element plays a role in providing information about expanded access that is similar to the role of Overall Recruitment Status in applicable clinical trials, indicating whether expanded access is currently available to patients.

(e) **Overall Recruitment Status**. This data element must be updated not later than 30 calendar days after a change in the overall recruitment status of the clinical trial.

(f) **Individual Site Status**. This data element must be updated not later than 30 calendar days after a change in status for any individual site.

(g) **Human Subjects Protection Review Board Status**. This data element must be updated not later than 30 calendar days after a change in Human Subjects Protection Review Board Status.

(h) **Primary Completion Date**. This data element must be updated not later than 30 calendar days after a clinical trial reaches its actual primary completion date.

(i) **Study Completion Date**. This data element must be updated not later than 30 calendar days after a clinical trial reaches its actual study completion date.

(j) **Responsible Party, by Official Title**. This data element must be updated not later than 30 calendar days after a change in either the name of the responsible party or in the responsible party's official title.

(k) **Responsible Party Contact Information**. Consistent with updates required to the Responsible Party data element, the Responsible Party Contact Information must be updated not later than 30 calendar days after a change in the responsible party or the responsible party's contact information.

(l) **Device Product Not Approved or Cleared by U.S. FDA**. This data element must be updated not later than 15 calendar days after a change in the approval or clearance status of one or more device products studied in the applicable clinical trial.

(m) **Record Verification Date**. This data element must be updated any time the responsible party reviews the complete set of submitted clinical trial information for accuracy, even if no other updated information is submitted at that time. The record verification date is intended to demonstrate when the information in *ClinicalTrials.gov* for a particular clinical trial was last checked for accuracy.

(n) Subsection 11.64(a)(1)(ii)(O) details that relevant clinical trial registration information be updated not later than 30 calendar days **after a protocol amendment is approved** by a human subjects protection review board, if the protocol is amended in such a manner that changes are communicated to participants in the applicable clinical trial or other clinical trial.

(o) Responsible parties must correct or address apparent **errors, deficiencies, and/or inconsistencies** within 15 calendar days (**clinical trial registration** information) or 25 calendar days (**clinical trial results** information) of notification sent by the Director.

- **NIH** – Same as FDAAA

- **ICMJE** – Not Required

Results Reporting

- **FDAAA** - Not later than 12 months after primary completion date; possible delay of up to an additional 2 years for trials of unapproved products or of products for which initial

FDA marketing approval or clearance is being sought, or approval or clearance of a new use is being sought.

- **NIH supported Study** - Not later than 12 months after primary completion date; possible delay of up to an additional 2 years for trials of unapproved products or of products for which initial FDA marketing approval or clearance is being sought, or approval or clearance of a new use is being sought.
- **ICJME** – Results not required

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

Food and Drug Administration Amendments Act of 2007, Section 801
42 Code of Federal Regulations Part 11

7) Attachments

None

8) Revision Dates