SOP: ClinicalTrials.gov Registration				
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1 PURPOSE

1.1 This policy ensures that the Principal Investigator (PI) and all research team members assisting in the conduct of clinical research are informed about their obligations and responsibilities as they pertain to Good Clinical Practices (GCP), the investigational plan, applicable regulations, guidance, and institutional policies.

1.2 This policy establishes the process to ensure required clinical trials are registered and remain in compliance with ClinicalTrials.gov, per their policies and requirements.

2 REVISIONS FROM PREVIOUS VERSION

2.1 None

3 POLICY

3.1 Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) requires Responsible Parties to register and submit summary results of Clinical Trials with ClinicalTrials.gov.

3.1.1 Registration is required for trials that meet the FDAAA 801 definition of an '"applicable clinical trial (ACT)" and were either initiated after September 27, 2007, or initiated on or before that date, and were still ongoing as of December 26, 2007. ACTs include the following:

3.1.1.1 Trials of drugs and biologics: controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation

3.1.1.2 Trials of devices: a study is an applicable device clinical trial if it meets the following criteria:

3.1.1.2.1 Prospective clinical study of health outcomes;

3.1.1.2.2 Comparing an intervention with a device product against a control;

3.1.1.2.3 Subject to section 510(k), 515, or 520(m) of the Federal Food, Drug and Cosmetic Act (FDC Act); and

3.1.1.2.4 A small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes are not required to be registered.

3.2 The National Institutes of Health (NIH) Policy on Dissemination of NIH-funded Clinical Trial Information applies to all NIH-funded clinical trials regardless of study phase, type of intervention, or whether they are subject to the Clinical Trial Registration and Results Information Submission regulation at 42CFR Part 11. The policy is effective for competing applications and contract proposals submitted on or after January 18, 2017, and states that all NIH- funded awardees and investigators conducting clinical trials will register and report the results of their clinical trials in ClinicalTrials.gov.

3.3 Effective January 1, 2015, all Medicare qualifying trials, including some phase I and device feasibility trials, are required to be registered into the ClinicalTrials.gov database. A ClinicalTrials.gov identifier (NCT number) is required on clinical trial related claims in order to receive payment. Patients should not be enrolled in a trial unless the NCT number is in place.

3.4 The International Committee of Medical Journal Editors (ICMJE) requires registration of any human research project that prospectively assigns human subjects to intervention or comparison groups to study the cause and effect relationship between a medical intervention and a health outcome.

3.5 Sponsors and PIs are responsible for registering ACTs with ClinicalTrials.gov. This is done in the ClinicalTrials.gov Protocol Registration and Results System (PRS).

3.6 Only an individual who is a member of the academic or research faculty can serve as the PI and Responsible Party for the purpose of registering and maintaining study records with ClinicalTrials.gov. Non-paid affiliates with a Human Resource approved P-86 appointment may not be designated to serve in these roles.

3.7 For investigator-initiated studies that are required to be registered at ClinicalTrials.gov, proof of registration is required to be provided to obtain final IRB approval.

3.7.1 Non-compliance with ClinicalTrials.gov reporting requirements could result in ICMJE participating journal publication delays or denials, institutional loss of NIH or HHS funding, and fines of up to $10,000 per day per instance of non-compliance.

3.7.2 Clinical Trials that are out of compliance with updating or reporting results may receive approval but will not have stamped consent documents released and therefore not be permitted to enroll subjects at the time of continuing review until proof that the record has been updated and released to the public site is provided. Investigators have two weeks to comply with ClinicalTrials.gov reporting requirements. Failure to comply with reporting requirements will result in notification of the investigator's dean or department chair and may also result in a for cause audit of the investigator's studies.

3.7.3 If a PI leaves Virginia Tech, modifications submitted to have another investigator assume PI responsibilities or closure reports will not be approved until proof that the responsible party has been updated in the ClinicalTrials.gov system.

4 RESPONSIBILITIES

4.1 The PI is responsible for making the initial determination if the study is an ACT, thus requiring registration and results information to be reported on ClinicalTrials.gov. This will be confirmed by a Human Research Protection Program (HRPP) staff at time of pre-review.

4.1.1 Documentation of this decision is recorded by the HRPP Office.

4.2 The PI is responsible for determining whether they are the Responsible Party using the following criteria.

4.2.1 For trials being conducted under a funding agreement, grant (e.g., NIH award) or department/internal funding, the funding recipient is considered the Responsible Party. Because the PI is in the best position to understand the research protocol, study results, and adverse events, the institution will designate the PI to assume the role of the Responsible Party.

4.2.1.1 In situations where Virginia Tech serves as the primary site for a clinical trial and the institution is determined to be the 'Responsible Party', the institution will designate this responsibility to the PI.

4.2.2 For studies initiated and written by an investigator at Virginia Tech, the PI of the study should be listed as the Responsible Party, whether listed as 'PI' or 'Sponsor Investigator'.

4.2.3 For most studies conducted by industry sponsors, the sponsor is considered to be the Responsible Party, and as such, the PI is not responsible for maintenance of the study's listing on ClinicalTrials.gov.

4.2.4 For multicenter and academic center trials, only the lead site (overall PI) typically bears responsibility for ClinicalTrials.gov reporting.

4.2.5 The Responsible Party has the sole authority to approve and release the record; all records must be reviewed and released by the PI. If the PI leaves Virginia Tech, please contact Virginia Tech PRS administrator to determine who should become the new Responsible Party.

4.2.6 The PI or his/her designee is responsible for registration and maintenance of their respective studies and determining whether he/she is the Responsible Party for such registration.

4.2.7 If the PI is not a Responsible Party for an ACT, the PI will be accountable for the following activities:

4.2.7.1 Ensuring that the informed consent document uses the necessary sentences required by 21CFR50.25(c)

4.2.7.2 Obtaining the NCT number from the sponsor or outside entity after confirming that they will be the Responsible Party for ClinicalTrials.gov registration

4.2.7.3 Assuring that the NCT number provided is added into Virginia Tech's IRB Protocol Management system

5 PROCEDURE

5.1 Once HRPP staff confirms that the study is an ACT the PI will receive notification that the study must be registered. This could happen prior to the approval of the study to avoid delays in registering the study.

5.1.1 Studies with approved consent language stating the study will be registered to ClinicalTrials.gov must register their study to ClinicalTrials.gov.

5.1.1.1 If it is determined that the study does not require registration per regulations and the PI decides not to register the study for publication or other purposes, then an amendment removing the ClinicalTrials.gov language must be approved by the IRB and consented subjects must be notified.

5.1.2 Studies that are not required to be registered per regulations or publication requirements may still be registered to ClinicalTrials.gov at the discretion of the PI.

5.2 Requests for a ClinicalTrials.gov account can be made by contacting the Virginia Tech PRS administrator at irb@vt.edu.

5.2.1 The request should contain the following information:

5.2.1.1 Requester's full name

5.2.1.2 Institutional email address

5.2.1.3 IRB number

5.2.1.4 Title of protocol

5.2.2 If the requestor is not the PI, an e-mail from the PI to the Virginia Tech PRS administrator is required to create or change access. Please note that the PI will need a ClinicalTrials.gov account to approve and release the record. You may request this at the same time if the PI does not have an account yet.

5.2.3 Once an account is created, the PI will be notified by the Virginia Tech PRS administrator and will receive an e-mail from the PRS) to modify the account password.

5.3 The Responsible Party is ultimately responsible for ensuring studies are registered with ClinicalTrials.gov, updated at required intervals, and released to the public database (Please see table below for timelines).

Event	Timeline Requirements	Notes
Registration	Prior to the enrollment of the first subject	A study is considered registered once the responsible party releases the record to PRS for review
Actively Enrolling Studies	Update/verification every 6 months	The record must be verified even if no changes need to be made
Studies Closed to Enrollment or Pending Results	Update/verification annually	The record must be verified even if no changes need to be made
Change in Study Status	Within 30 days of status change	

Results Submission	No later than one year after the primary completion date	Delayed submission of results is permitted in certain circumstances. See 42CFR11.44 for details

5.3.1 The Virginia Tech PRS administrator will contact the PI if their protocol record is delinquent and needs to be updated.

5.3.2 If the protocol record remains delinquent two weeks after the first notice, a second notification will go out to the PI, and to the PI's department chair.

5.3.3 If the protocol record remains delinquent one month after the initial contact without activity/progress, the Vice President of Research and Innovation (VPRI) will be notified of the non-compliance.

5.4 There are potential legal consequences for a Responsible Party who does not comply with the registration requirements. These may include civil or criminal judicial actions, civil monetary penalty actions, and grant funding actions. As such, the HRPP and IRB may refer continued incidents of non-compliance to the VPRI for possible sanctions, which may include withdrawal or suspension of research privileges, embargo of the data for research or publication, financial penalties, disciplinary action, or other corrective action deemed appropriate by the VPRI, in consultation with the relevant dean and/or head of the PI's department.

5.4.1 Virginia Tech employees who do not comply with the FDAAA requirements may face financial penalties, withholding of funds, and sanctions imposed by the FDA.

5.4.2 Virginia Tech employees who do not comply with NIH requirements may face withholding of cash payments, disallowing cost for an activity, suspending or terminating either in part or whole the current award, withholding a future award, and having a non-compliance notice publicly available.

5.4.3 Virginia Tech employees who do not comply with ICMJE requirements may face publication restrictions in an ICMJE affiliated journal.

6 DEFINITIONS

6.1 Applicable Clinical Trial (ACT)

6.1.1 Device Clinical Trial – A device clinical trials is (1) a prospective clinical study of health outcomes comparing an intervention with a device product subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360(k), 21 U.S.C. 360e, 21 U.S.C. 360j(m)) against a control in human subjects (other than a small clinical trial to determine the feasibility of a device product, or a clinical trial to test prototype device products where the primary outcome measure relates to feasibility and not to health outcomes); (2) a pediatric postmarket surveillance of a device product as required under section 522 of the FD&C Act (21 U.S.C. 3601); or (3) a clinical trial of a combination product with a device primary mode of action under 21 CFR Part 3, provided that it meets all other criteria of the definition under this part.

6.1.2 Drug Clinical Trial - A drug clinical trial is a controlled clinical investigation, other than a phase 1 clinical investigation, of a drug product subject to section 505 of the FD&C Act (21 U.S.C. 355) or a biological product subject to section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262), where "clinical investigation" has the meaning given in 21 CFR 312.3 and "phase 1" has the meaning given in 21 CFR 312.21. A clinical trial of a combination product with a drug primary mode of action under 21 CFR Part 3 is also an applicable drug clinical trial, provided that it meets all other criteria of the definition under this part.

6.2 International Committee of Medical Journal Editors (ICMJE) – The ICMJE is a group of medical journal editors who meet annually and independently develop recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals.

6.3 ClinicalTrials.gov Identifier (NCT number) - A unique identification number assigned to a clinical trial registered on ClinicalTrial.gov referred to as the NCT number. It is assigned after the responsible party has released (submitted) the record and the ClinicalTrial.gov staff has completed their review.

6.4 Principal Investigator (PI) – The PI is the individual designated in the grant application and approved by the Virginia Tech PRS administrator, who is responsible for the scientific and technical direction of the project.

6.5 Protocol Registration and Results System (PRS) - The PRS is a web-based system used to submit study data to ClinicalTrial.gov. The Virginia Tech PRS administrator is a HRPP staff member that has oversight of Virginia Tech's ClinicalTrials.gov account.

6.6 Responsible Party - The responsible party is the sponsor of the clinical trial, as defined in 21 CFR 50.3; or the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as 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 under this part for the submission of clinical trial information. For a pediatric postmarket surveillance of a device product that is not a clinical trial, the responsible party is the entity who FDA orders to conduct the pediatric postmarket surveillance of the device product.

6.7 Record Owner – The record owner creates the study record in PRS; this person can maintain the study record or give access to another user who can maintain the record on their behalf.

7 MATERIALS

7.1 None

8 REFERENCES

8.1 Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA801)
8.2 42 CFR §11
8.3 Section 402(j)(5)(A) of the Public Health Service Act42 CFR §11.66(c)
8.4 21 CFR §50.25(c)
8.5 42 CFR §11.44
8.6 42 CFR §11.66