Clinical Trials Registration

Policy Type: Administrative
Responsible Office: Office of Research, Office of Sponsored Programs
Initial Policy Approved: 12/09/2013
Current Revision Approved: 12/09/2013

Policy Statement and Purpose

This Policy describes the registration and results reporting requirements for all clinical trials in the ClinicalTrials.gov public registry/database in support of the International Committee of Medical Journal Editors (ICMJE) publication policy, as mandated by federal law and in compliance with the National Institute of Health (NIH) funding requirements.

Virginia Commonwealth University requires preregistration of all clinical trials regardless of funding in the ClinicalTrials.gov registry not only as an educational tool for human subject volunteers but also as a mechanism to ensure continuity in the research enterprise, which supports research integrity through the dissemination of research results, whether positive or negative.

VCU follows the preregistration requirements of the ICMJE publication policy for all clinical trials to ensure continued protection of academic freedom, meeting the results reporting requirements and grant certification requirements, and all other requirements of compliance under the law.

Background:

Federal Law

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA) was passed. The Act expands the types of clinical trials required to be registered in the ClinicalTrials.gov registry originally created under the Food and Drug Modernization Act of 1997 and includes a requirement for the submission of results for public information.

Under Title VIII of FDAAA (Public Law 110-85), Applicable Clinical Trials, regardless of funding source, are required to be registered and results reported by the Responsible Party in the ClinicalTrials.gov registry maintained by the National Library of Medicine (NLM). Applicable Clinical Trials subject to FDAAA generally include controlled interventional studies (with one or more arms) of drugs, biological products or devices which are subject to FDA regulation. FDA Regulation generally means that the trial has one or more sites in the U.S, involves a drug, biologic, or device that is manufactured in the US (or its territories), or is conducted under an investigational new drug application (IND) or investigational device

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exemption (IDE). The law specifies two types of Applicable Clinical Trials: Applicable Drug Clinical Trials and Applicable Device Clinical Trials. Additional elaboration from NIH can be found under the related documents section of this policy.

In accordance with Title VIII, the law mandates that studies meeting the definition of an Applicable Clinical Trial must be registered no later than 21 days after enrollment of the first study subject and results reported no later than one year after the Primary Completion Date whether the study is completed or is terminated. The law applies to those trials initiated on or after September 27, 2007 or those trials ongoing as of December 26, 2007. Additional information on how to identify an Applicable Clinical Trial can be found under the related documents section of this policy.

Results reporting may be delayed for Applicable Clinical Trials which are completed prior to the initial approval or clearance of an investigational drug, biologic or device by the Food and Drug Administration (FDA) or if the trial is investigating a new use of an FDA approved drug, biologic or device and the manufacturer is sponsoring the study and has filed an application to the FDA for approval or clearance. However, results must be posted within 30 days of receiving such approval or clearance.

Non-compliance with FDAAA may have severe consequences for the Responsible Party/University including but not limited to civil monetary penalties of up to $10,000 per day and withholding of federal grant funding.

**International Committee of Medical Journal Editors Requirements:**

As a prerequisite for publication in any journal subscribing to the ICMJE publication policy, the ICMJE instituted the requirement that clinical trials beginning on or after July 1, 2005 be registered on a publicly accessible internet site (such as ClinicalTrials.gov) prior to enrollment of the first study subject. In 2008, the ICMJE adopted the World Health Organization’s definition of a “clinical trial” which expanded the original registration requirement to cover Phase I studies.

Non-compliance with the ICMJE’s publication policy could result in rejection of manuscripts for publication. Consequently, this could negatively impact the investigator’s ability to obtain or retain funding, jeopardize student support under the research, or compromise the university’s ability to meet the terms and conditions of the award with the funding entity.

**National Institute of Health – Certification of Compliance Requirements**

NIH requires certification of compliance with FDAAA in competing and non-competing grant applications for those Applicable Clinical Trials funded in whole or in part by a grant from any agency of the Department of Health and Human Services, including NIH, the FDA or the Agency for Healthcare Research and Quality.

Non-compliance with this requirement may cause a disallowance of current funding or a loss of future funding.

In further support of the law, the NIH website contains the following statement: “The NIH encourages registration and results reporting for all NIH-supported clinical trials, regardless of whether or not they are subject to FDAAA.”
There are distinct requirements which VCU must follow for compliance with clinical trial registration and results reporting. Not all clinical trials which are registered on ClinicalTrials.gov must have results reported. To differentiate between these, VCU follows the ICMJE requirements for clinical trial registration purposes and the requirements under FDAAA for results reporting purposes based on the definition of an Applicable Clinical Trial.

**COMPLIANCE**

Noncompliance with this policy may result in disciplinary action up to and including termination. VCU supports and environment free from retaliation. Retaliation against any employee who brings forth a good faith concern, asks a clarifying question, or participates in an investigation is prohibited.

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**Who Should Know This Policy**

All individuals involved in the conduct of clinical trials are responsible for knowing this policy and familiarizing themselves with its contents and provisions.

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**Definitions**

**Applicable Clinical Trial**

The term used under FDAAA to describe an applicable drug clinical trial or an applicable device clinical trial as further defined below:

1. **Applicable Drug Clinical Trial** - “a controlled clinical investigation, other than a Phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of the Public Health Service Act.”
Applicable Device Clinical Trial - “(I) a prospective clinical study of health outcomes comparing an intervention with a device subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act against a control in human subjects (other than 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); and (II) a pediatric post-market surveillance as required under section 522 of the Federal Food, Drug, and Cosmetic Act.”

Clinical Trial (as adopted by ICMJE)
For purposes of this policy, this term takes the meaning as adopted by the ICMJE. A clinical trial is “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”. A health-related intervention includes “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).”

ClinicalTrials.gov
A national public registry and results reporting database for clinical trials developed by the National Institutes of Health through the National Library of Medicine in collaboration with the Food and Drug Administration as a result of the Food and Drug Administration and Modernization Act of 1997 (FDAMA). It provides public access to information about clinical trials conducted in the United States and internationally regardless of funding source.

Principal Investigator
a) The individual with final responsibility for the conduct of research or other activity described in a proposal or an award; b) the individual with fiduciary responsibility for an award’s management. Usually these are the same individual. However, VCU has a requirement that the fiduciary responsibility vest in a VCU employee, so on occasion they may be different.

Primary Completion Date
The date the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome. Submission of initial results reporting is required no later than one year after this date for Applicable Clinical Trials.

Protocol Registration System (PRS)
A Web-based data entry system supported by ClinicalTrials.gov used for the registration of clinical studies and the submission of results and adverse event information for registered studies.

Responsible Party
As required under FDAAA, the Responsible Party is the sponsor of the clinical trial (as defined in 21 CFR 50.3) and is required to register clinical trials and provide results information for registered trials. The university is the Responsible Party for all VCU investigator-initiated studies. The Responsible Party releases the record to ClinicalTrials.gov for registration.
**Sponsor**
A person or entity who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

**Sponsor-Investigator**
Under Title 21 of the Code of Federal Regulations, the term Sponsor-Investigator is defined as an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

**Contacts**
The Office of Sponsored Programs officially interprets this policy. The Office of Sponsored Programs is responsible for obtaining approval for any revisions as required by the policy Creating and Maintaining Policies and Procedures through the appropriate governance structures. Please direct policy questions to the Office of Sponsored Programs.

**Procedures**

The university is the Responsible Party with respect to registration of investigator initiated studies regardless of funding source (NIH, industry funded, internally funded) and has established an organizational account with the Protocol Registration System of ClinicalTrials.gov to register these types of clinical trials. The university appoints an administrator to review and process actions required of the university.

The Principal investigator is responsible for ensuring the registration of his/her clinical trial prior to enrollment of study subjects using the following procedures:

1. **Request for Account Create**
   
The Principal Investigator or his/her designee shall complete an electronic account create request form to establish an individual account. The individual submitting the request will be considered the record owner for any records created under this account. The request should include the individual’s contact information as well as contact information for anyone who needs access to the protocol records. Once an account has been created, the record owner will receive an automated email reply containing a link to the registration site and login information.

2. **Registration of Protocols on Clinical Trials.gov**
Using the Organization name, user name and password provided by the university administrator, registration will be accomplished through a menu-driven Protocol Registration System (PRS) on the following site:  [https://register.clinicaltrials.gov](https://register.clinicaltrials.gov)

Once all of the information has been entered in the PRS record and marked as completed, an automated email will be sent to the university administrator for review.

The administrator will review the record and may ask the record owner for some additional information prior to release of the record. Upon completion of the review, the administrator will approve and release the record to ClinicalTrials.gov where the PRS Team will review the record for quality control purposes prior to posting on the ClinicalTrials.gov website.

### 3. Updating and Results Reporting Requirements

The Principal Investigator is responsible for ensuring that their PRS records are updated for all registered clinical trials at least every six months or earlier if there is a change in the status of the trial. Each time a record is updated, an automated email will be sent to the administrator for review, approval and re-release of the record.

The Principal Investigator is responsible for ensuring that their PRS record is updated to add results and adverse event information for public release in accordance with FDAAA for Applicable Clinical Trials no later than one year after the Primary Completion date. Once information has been added to the protocol record and marked as completed, an automated email will be sent to the administrator for review, approval and re-release of the record.

Before final submission to the public site can occur, the PRS Team will review any updates to the record prior to its re-release and will either submit the record for posting to the ClinicalTrials.gov site or will indicate comments which need to be addressed. The Principal Investigator is responsible for ensuring that all review comments are addressed to facilitate posting on the public site. For questions regarding posting of results, please contact ClinicalTrials.gov at register@clinicaltrials.gov

### 4. Delayed Submission of Results

Submission of results for FDA regulated Applicable Clinical Trials can only be delayed under very specific circumstances. Delayed submission of results must be requested through a certification process under the following condition: “if the responsible party is seeking initial approval or clearance of a drug or device or if the manufacturer of a drug or device has filed or will file within a year an application for approval or clearance of a new use (which is also the use studied in the clinical trial)”.

### 5. Certification of Compliance Requirements for Grants

The Principal Investigator is responsible for ensuring that the appropriate certification of compliance with FDAAA is included in competing and non-competing grant applications for Applicable Clinical
Trials funded in whole or in part by a grant from the following agencies: The Department of Health and Human Services, including NIH, the FDA or the Agency for Healthcare Research and Quality.

Certification includes the following information: the ClinicalTrials.gov registration number, also referred to as “National Clinical Trial (NCT) number,” the title of the clinical trial and the identification and contact information for the Responsible Party. For proposed trials not yet registered, a statement indicating the project will include an Applicable Clinical Trial needing registration is required at the time of grant submission.

6. Institutional Review Board Oversight

The Principal Investigator is responsible for ensuring that Institutional Review Board oversight is maintained until study completion and results reporting requirements for Applicable Clinical Trials have been satisfied.

Forms

1. E-CT.gov Account Create Request Form
   http://www.research.vcu.edu/forms/e-ct_account_creation_form.htm

Related Documents

1. The Federal Drug Administration Amendments Act (FDAAA) of 2007

2. ICMJE Publication Policy and Frequently Asked Questions about Clinical Trial Registration
   http://www.icmje.org/publishing_10register.html
   http://www.icmje.org/faq_clinical.html

3. Identifying an Applicable Clinical Trial under FDAAA
   http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf

4. NIH Elaboration of Definitions - Applicable Clinical Trial

5. ClinicalTrials.Gov (general information)
   http://clinicaltrials.gov/
Revision History

This policy supersedes the following archived policies:

Approval/Revision Date: Clinical Trials Protocol Registration, 3/3/2009

FAQs

1. When does my study need to be registered?

Studies need to be registered and the record released to ClinicalTrials.gov prior to enrollment of the first study subject to comply with ICMJE requirements.

2. What is the difference between the registration and reporting requirements for ICMJE and FDAAA?

VCU follows the ICMJE requirements for registration of all clinical trials prior to enrollment of the first subject. The ICMJE does not have a results reporting requirement. VCU follows the results reporting requirement under the FDAAA law of 2007 which requires that a subset of clinical trials defined as Applicable Clinical Trials be registered and have initial results reported no later than 12 months from the Primary Completion Date of the trial.

3. Who can assist me with my registration?

Please contact OSPRED@vcu.edu if you need assistance with account set up information or have questions about registering a study.
4. Does my study need Institutional Review Board approval prior to registration?

Studies which have not yet begun recruiting may be registered prior to Institutional Review Board approval; however, the record must be updated with the approval information prior to enrollment of the first subject.

5. How can I determine if my study is an applicable clinical trial subject to FDAAA?

Please see “Identifying an Applicable Clinical Trial under FDAAA” (Item #3 in Related Documents Section) and/or the following table

Answer the following questions. If you answer “yes” to all questions, your study will be considered an Applicable Clinical Trial (ACT) for results reporting purposes:

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
<th>Clarification/additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Timeline. Was your study either Initiated after September 27, 2007?</td>
<td></td>
<td></td>
<td><a href="http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf">http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf</a></td>
</tr>
<tr>
<td>OR Initiated on or before September 27, 2007 and ongoing as of December 26, 2007?</td>
<td></td>
<td></td>
<td>Interventions which modify a health related outcome. Observational studies where the intervention is given as part of clinical care and not assigned by the protocol are not considered ACT’s.</td>
</tr>
<tr>
<td>2. Interventional vs Observational Are participants assigned to an intervention through the study protocol?</td>
<td></td>
<td></td>
<td>FDA jurisdiction – conducted under an IND/IDE or at least one site is in the US</td>
</tr>
<tr>
<td>3. Is your study under FDA jurisdiction/regulation?</td>
<td></td>
<td></td>
<td>FDA definitions apply. Devices include diagnostic devices such as x-ray and CT scans. <a href="http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm?q2=a+drug+or+biologic#">http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm?q2=a+drug+or+biologic#</a></td>
</tr>
<tr>
<td>5. Is your study other than (a) a small feasibility or pivotal device trial or (b) a phase 1 drug/biologic trial</td>
<td></td>
<td></td>
<td>Phase 1 studies and small feasibility device studies are not considered ACT’s.</td>
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</table>