I. Background

The Food and Drug Administration Amendments Act ("FDAAA") of 2007 expands the scope of registration of clinical trials at Clinical Trials.gov, increases the amount of information that must be provided at the time of registration, requires the eventual inclusion of trial results, and imposes penalties for noncompliance.

As of 2005, most medical journals, including International Committee of Medical Journal Editors ("ICMJE") member publications, require as a condition of consideration for publication, the prospective registration of certain clinical trials in a public trials registry. Failing to register makes the results of the trial ineligible for publication in the ICMJE member journals.

II. Policy

A. Which clinical trials must be registered under the new law?

1. The FDAAA requires the registration of the following types of studies:

   a) Controlled, clinical investigations of drugs and biologics subject to FDA regulation, other than Phase I trials;
   b) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies and pediatric post market surveillance.

2. The ICMJE policy goes beyond the FDAAA requirements by promoting registration of “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,” including Phase I trials.
a) 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).
b) Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.

3. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

4. The ICMJE member journals began implementing the expanded definition of clinically directive trials for all trials that begin enrollment on or after July 1, 2008. Those who are uncertain whether their trial meets the expanded ICMJE definition should err on the side of registration if they wish to seek publication in an ICMJE journal. The ICMJE secretariat office does not review specific studies to determine whether registration is necessary. If researchers or others have questions about the need to register a specific study, they should err on the side of registration or consult the editorial office of the journal in which they wish to publish.

5. For additional information about which clinical trials should be registered, refer to:


B. Who is responsible for registering a trial?

1. The FDAAA defines the entity responsible for registering a trial as the “responsible party.” The responsible party is defined as the sponsor of the clinical trial (as defined in 21 CFR 50.3) or the principal investigator of the clinical trial if so designated by a sponsor, grantee, contractor, or awardee. ClinicalTrials.gov prefers that the sponsor register the trial, as opposed to the principal investigator, whenever possible.
a) For investigator-initiated trials, the lead principal investigator should register each clinical trial affected by the FDAAA and ICMJE policy.

b) **For sponsor-initiated trials, the sponsor is responsible for registration.** Contact the sponsor to ensure that the sponsor has registered the clinical trial with ClinicalTrials.gov.

c) For trials sponsored or funded wholly or in part by the NIH, the lead principal investigator is responsible for registration.

d) For trials associated with Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications with the FDA, the IND/IDE holder is responsible for registration.

e) The sponsor, grantee, contractor, or awardee may designate the principal investigator of a clinical trial as the responsible party, 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 the requirements for submitting information under the law.

f) If it is unclear who is responsible for registering an applicable clinical trial, investigators should consult with the sponsor, funding agency, and/or other study investigators to define who the responsible party will be.

2. Before investigators register a sponsored trial, they should search the ClinicalTrials.gov site to be sure that the trial has not already been registered.

C. **When must a trial be registered?**

1. Trials initiated after September 27, 2007 or trials that are “ongoing” as of December 26, 2007 must be registered in full by: the later of December 26, 2007 or twenty one days after the first patient is enrolled. Existing ICMJE policy requires that the principal investigator register the trial before beginning new subject enrollment.

2. Trials that were “ongoing” as of September 27, 2007 and do not involve a “serious or life threatening disease or condition,” must be registered by **September 27, 2008**.

3. Trials that were “ongoing” as of September 27, 2007, do involve a “serious or life threatening disease or condition,” and are completed by December 26, 2007, are not subject to the FDAAA requirements, though they are subject to pre-existing FDAMA requirements.

4. “Ongoing” in this context means a trial had one or more subjects enrolled, but had not examined the final subject or provided the final subject and intervention for the purposes of final collection of data for the primary outcome as of September 27, 2007.
5. For trials already registered in compliance with ICMJE policy, minimal additional data is required to meet the FDAAA requirements. Additionally, once registered, the data should be updated during the course of the trial. The principal investigator should work collaboratively with sponsors of multi-site trials to avoid duplication of efforts.

D. Where should a clinical trial be registered?

The trial should be registered through the ClinicalTrials.gov protocol registration systems (PRS). The ClinicalTrials.gov PRS is a service of the US National Institutes of Health (NIH), provided through its National Library of Medicine (NLM) that meets the FDAMA, FDAAA, and ICMJE requirements. The site can be accessed on-line at http://prsinfo.clinicaltrials.gov.

E. Does the registration listing need IRB approval?

In accordance with guidance from the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA), the clinical trial listing does not require IRB approval. Direct advertising for subject studies, however, does require prospective IRB approval because it is considered to be part of the informed consent and subject selection process.

F. What happens if you do not register your clinical trial?

1. The FDAAA imposes penalties for failure to register or for providing false or misleading information may include civil monetary penalties and for federally-funded trials, the withholding or recovery of grant funds.

2. Additionally, researchers who have not registered or have improperly registered their trials take the risk that their manuscripts may not be reviewed and/or accepted by the ICMJE members and other medical journals.

G. What about submitting information regarding trial results? ClinicalTrials.gov requires submission of results. Please see Section III(D) for submission of clinical trial results.

III. Procedure

A. How does a principal investigator register his/her trial?
1. To register a trial, proceed to the ClinicalTrials.gov PRS site at http://prsinfo.clinicaltrials.gov. Under “Account Application Process”, choose “Apply for an individual account” (instructions are provided in section “B” below). Alternatively, a department or unit may establish an organizational account with an individual identified as the account’s PRS Administrator.

2. The ClinicalTrials.gov PRS site includes a guided tour, definitions, frequently asked questions, and a list of the data elements needed for registration. If you have questions or encounter problems in the registration process, contact register@clinicaltrials.gov.

B. Instructions to apply for an Individual Account


2. The “Getting a PRS Individual Account” page will open and ask six questions before starting the account application process. If you get to question 6, “Is your organization already registered with PRS?” answer “no” and select “Apply for a PRS Account.”

3. The “Individual Account Application” page will open. First, read and accept/not accept the terms and conditions for submitting data to clinicaltrials.gov. If you accept these terms and conditions, you will need to complete the following fields in the application:

   a) Sponsor information - if the clinical trial is sponsored, the sponsor’s name and contact information should be entered into this section. If the clinical trial is investigator-initiated, enter the name and contact information for the office at the university who can verify the Principal Investigator’s affiliation with Tulane University (this is usually the principal investigator’s department):

   - Registering IND/IDE trials? (Select “yes” or “no”)
   - Type of Organization –
   - Organization name –
   - Organization address – (“List the address for the sponsor/office listed directly above”)
   - Organization Abbreviations and Acronyms –
b) Investigator Information:

- Investigator Name – (List principal investigator’s name)
- Affiliation (if not the sponsor) – (Do not list anything in this field if the investigator is affiliated with Tulane, which is the sponsor)
- Investigator Phone – (List principal investigator’s phone number)
- Investigator Email – (List principal investigator’s email address)

c) Regulatory Information:

- Regulatory Authority – (List Tulane University Biomedical IRB as the regulatory authority.)
- Regulatory Authority Address – (If FDA is listed as the regulatory authority, use the following address: 5600 Fishers Lane, Rockville, MD 20857. If the Tulane Biomedical IRB is listed as the regulatory authority use the following address: Human Research Protection Office; Tidewater Bldg., Suite 1705, TW36; 1440 Canal Street; New Orleans, LA 70112)
- When finished, select “Submit Application” at the bottom of the application page.
- Within approximately 1 – 2 days you will receive an email from ClinicalTrials.gov Registration that gives you a user name and password and instructs you to login and change your password as soon as possible. The email will also provide the PRS web site address for the registration process.

C. Instructions to Register a Clinical Trial (once you have received your login information):

1. Once you have received your login information, to register a clinical trial, login to the PRS web site for the registration process. This will take you to the Main Menu page that provides you with several options, including “Change Password” under “User Account”.

The official version of this information will only be maintained in an on-line web format. Any and all printed copies of this material are dated as of the print date. Please make certain to review the material on-line prior to placing reliance on a dated printed version.
2. Under “Help” you will receive detailed instructions by selecting “User’s Guide” or definitions of the different fields by selecting “Data Element Definitions”.

3. To register a trial, select “Create” under “Protocol Records”

4. One section of the registration form asks for information regarding human subjects review. The following are suggested entries for these fields.
   a. Board Approval Number – *List the IRB Protocol number assigned to your research*
   b. Board Name – Tulane University Biomedical IRB
   c. Board Affiliation – Tulane University
   d. Contact Information: Roxanne Johnson, Director; Email: rjohnson@tulane.edu; Phone: (504) 988-2665; Human Research Protection Office; 1440 Canal Street, Suite 1705; New Orleans, LA 70112.

5. Oversight Authorities – *List United States Food and Drug Administration as the oversight authority if the research involves an investigational drug, device or biologic. Otherwise, list United States: Institutional Review Board as the oversight authority.*

6. Please use “Tulane University” when asked for your affiliation or facility.

7. The complete list of required data elements by the FDAAA and definitions is available at the ClinicalTrials.gov site: [http://prsinfo.clinicaltrials.gov/definitions.html](http://prsinfo.clinicaltrials.gov/definitions.html). It is suggested that you print the definitions for ease in completing the clinical trial registration process. The clinical trial registration process will take approximately 1 hour, and it will be helpful to have the protocol, informed consent document, and IRB approval (if available) on hand. Note that the clinical trial registration system offers the option to save data if you do not have time to complete the entire process.

D. **What about submitting information regarding trial results?**

1. The following is the current process for submission of information about the trial results:
   a) Log in to the PRS
   b) Click [Modify] on the *Main Menu* (under Protocol Records)
   c) Click [Edit] next to the record for which results data are to be entered
d) Click [Enter Results] (below second [Edit], under the "IND/IDE Protocol?" data field) in the *Edit Protocol Record* screen.

e) Carefully review the information from the protocol section that will be used to pre-populate data elements in the results section.

- If there are any errors, click [Cancel] and correct the data in the protocol section.
- Note that at least one Primary Outcome Measure must be provided in the protocol section in order to create a results section.

f) Click [OK] to create the results section of the PRS record.

2. Note: After the results section is created, any changes to Arms/Groups must be made in both the protocol and results sections of the record to maintain consistency. However, because the Primary and Secondary Outcome Measure will be accessible only through the results section, any changes to these data elements will also be displayed in the protocol section of the record at ClinicalTrials.gov.