

**The Carle Foundation
IRB Policy 1101**

Subject	Clinical Trials Registration		
Approval	Dec 2006	Review	Sep 2010
Purpose	To provide guidance for the registration		
Revision	Jun 2009		

What Kinds of Trials Must be Registered?

1. In 2005, most medical journals and the International Committee of Medical Journal Editors (ICMJE) adopted a policy requiring the registration of certain types of clinical trials in a public registry in order to receive consideration for publication. This registration is required to take place before the commencement of the clinical trial.
2. In 2007, the US Food and Drug Administration Amendments Act (FDAAA) amended the Public Health Service Act to expand the scope of clinical trials that must be registered in ClinicalTrials.gov. It also increased the number of registration fields that must be submitted, requires certain information about the results to be included and sets penalties for noncompliance.
3. The FDA Amendments Act of 2007 requires “applicable clinical trials” to be registered. These trials generally include:
 - a. **Trials of Drugs and Biologics:** Controlled, clinical investigations, other than phase I investigations, of a product subject to FDA regulation.
 - b. **Trials of Devices:** Controlled trials with health outcomes of devices subject to FDA regulations (other than small feasibility studies) and pediatric post-market surveillance.
4. The ICMJE policy expands on this by stating that all “clinically directive” trials – trials that test a clinical hypothesis about a clinical outcome, must be registered. This would include any clinical trial that “prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome”. This requirement does not apply to phase I trials, but does include phase II and phase III trials.

Who is Responsible for Registration?

1. The task of registration falls upon the designated “responsible party” for a clinical trial. The “responsible party” is defined as follows:
 - a. The sponsor of the clinical trial.
 - b. The principal investigator (PI) of such clinical trial if designated as the “responsible party” by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial and has sufficient data rights.
2. **Investigator-initiated Trials:** For PI-initiated trials, the PI is responsible for the registration of trials.
3. **Multi-Site:** For multi-site trials, the sponsor or lead site is responsible for the registration of the trial. For IND and IDE studies, the responsibility falls upon the holder of the IND or IDE.
4. **NIH-Sponsored:** For NIH-sponsored extramural research, where there is no IND or IDE holder, the funding recipient may be the “responsible party”. The NIH would not be classified as the “responsible party”.
5. Before investigators register a sponsored trial, they should search <http://www.clinicaltrials.gov/> to make sure that the trial has not already been registered.

Timing of Registration

1. Trials initiated after 9/27/2007, or trials initiated before that date and ongoing* on 12/26/2007 that involve a “serious or life threatening disease or condition,” must be registered in full by: the later of 12/26/2007 or 21 days after the first patient is enrolled.
2. Trials that were initiated before 9/27/07 that are ongoing* as of 12/26/2007, and which do **not** involve a “serious or life threatening disease or condition,” must be registered by 9/27/2008.
 - a. ***Ongoing** means a trial had one or more patients enrolled, but had not reached its “completion date,” meaning, examined the final subject or provided the final subject an intervention for the purposes of final collection of data for the primary outcome.
3. The study does not have to be approved by the local IRB at the time of registration. However, if there is direct advertising for study subject, that will need to have IRB approval.
4. ICMJE requires the registration of a clinical trial before subject enrollment is initiated.
5. **Trial registration data should be updated during the course of the trial.**

Where to Register?

1. Clinical trials are registered through the ClinicalTrials.gov “Protocol Registration System” (PRS). The ClinicalTrials.gov PRS is a service that meets the registration requirements of the FDA and the ICMJE. This site can be accessed online at <http://prsinfo.clinicaltrials.gov>.

What Information is Needed for Registration?

1. There are many details that must be included for registration to be completed. The initial information falls into the following primary fields:
 - a. Titles and Background Information
 - b. FDA Information – IND/IDE
 - c. Human Subjects Review
 - d. Sponsors
 - e. Study Description
 - f. Status (recruiting, closed to enrollment, completed, expanded access)
 - g. Study Design including Arm, Groups and Interventions, primary and secondary measures
 - h. Conditions and Keywords- Words or phrases that best describe the protocol
 - i. Eligibility requirements
 - j. Protocol Location, Contact and Investigator Information
 - k. Related references and links
2. A full description of all items found on the ClinicalTrials.gov registration application can be found online at: <http://prsinfo.clinicaltrials.gov/definitions.html>.
3. The current information needed for registration on ClinicalTrials.gov covers the requirements set forth in the IMCJE policy. A full list of the required elements for IMCJE can be found at the end of the article at: http://www.icmje.org/clin_trialup.htm.
4. The submission of information about the trial results will be required, but the content of and format for this information has not been finalized.
5. **FDA 3674**
 - a. In addition to registration on the ClinicalTrials.gov PRS system, the FDA requires the completion and submission of form FDA 3674 which certifies that the clinical trial and its investigators are in compliance with 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act. A copy of this form can be found online at: <http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3674.pdf>.

How to Register

1. Registration of a trial can be performed at the ClinicalTrials.gov PRS site at <http://prsinfo.clinicaltrials.gov>. Under the “Account Application Process” heading, click on “Apply for an individual account”. Alternatively, a department or unit can establish and organizational account with an individual identified as the account’s PRS Administrator.
2. Once the PRS account has been created, trials can be registered. The ClinicalTrials.gov PRS site includes information and other resources that aid in the registration process. For a full list and description of all of the elements on the trial registration form, see the link provided above. If questions arise or if problems with the registration process are encountered, contact register@clinicaltrials.gov.

What Happens If You Do Not Register?

1. The FDA Amendments Act of 2007 imposes penalties for failure to register or for providing false or misleading information. These penalties may include civil penalties, monetary penalties, and for federally-funded trials, and 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 accepted by medical journals.

References

For more information about clinical trial registration, refer to the following resources:

“Is This Clinical Trial Fully Registered?: A statement from the International Committee of Medical Journal Editors” online at: http://www.icmje.org/clin_trialup.htm.

Fact Sheet “Registration at ClinicalTrials.gov: As Required by Public Law 110-85, Title VII online at: <http://prsinfo.clinicaltrials.gov/s801-fact-sheet.pdf>.

Guidance from NIH Office of Extramural Research “Guidance on New Law (Public Law 110-85) Enacted to Expand the Scope of ClinicalTrials.gov Registration” online at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>.

The full text of US Public Law 110-85 can be found online at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf.

Protocol Registration System: Frequently asked questions: <http://prsinfo.clinicaltrials.gov/faq.html>.

Public Law 110-85, Sec 801 at:

http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf.

Approval On File

*Approved by IRB Board Aug 2010

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