Registration of Clinical Trials at ClinicalTrials.gov

Background
ClinicalTrials.gov is a databank or registry of federally and privately supported clinical trials conducted in the United States and worldwide. It is managed by the National Library of Medicine within the National Institutes of Health (NIH). ClinicalTrials.gov is the result of a federal law requiring that clinical trials be registered to improve public access to information about clinical research (Public Law 110-85). This guidance document provides information about registration requirements.

Federal (FDA) Requirements
All applicable clinical trials must be registered at ClinicalTrials.gov, regardless of funding source. Applicable drug and device clinical trials are defined as follows:

Drugs and Biologics: A controlled clinical investigation, other than a Phase 1 clinical investigation, of a drug or biologic product subject to FDA regulation.

Medical Devices: A prospective clinical study of health outcomes comparing an intervention with a medical device against a control.

Registration is not required for small trials to determine the feasibility of a device or to test prototype devices where the primary outcome measure relates to feasibility, and not to health outcomes.

ICMJE Requirements
As of 2005, most medical journals, including member publications of the International Committee of Medical Journal Editors (ICMJE), require registry as a condition of publication. Thus, researchers who plan to publish in an ICMJE member journal must meet ICMJE guidelines for clinical trial registration.

ICMJE defines an applicable clinical trial as follows:

“…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.

Be aware that the ICMJE definition of an applicable clinical trial is much broader than the FDA’s. ICMJE requires registration of controlled and uncontrolled drug, biologic, and device studies as well as dietary interventions and behavioral treatments related to health outcomes.

1 See http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf for more details about the definition of applicable clinical trials.
2 Many non-ICMJE medical journals have adopted similar registration requirements. Researchers are encouraged to consider publication plans prior to initiating clinical trials to ensure they meet journal requirements.
3 http://www.icmje.org/faq_clinical.html
For both FDA and ICMJE, purely observational studies (those in which the assignment of the health-related intervention is not at the discretion of the investigator) do not require registration.

**Frequently Asked Questions**

**When must applicable clinical trials be registered?**
Federal regulations require that trials be registered no later than 21 days after enrollment of the first participant. However, researchers should be aware that ICMJE requires registration prior to enrollment of any subjects, and member journals may decline publication articles from studies that were not registered in accordance with this requirement.

Results from applicable clinical trials must be reported to ClinicalTrials.gov no later than 12 months after the primary completion date. The primary completion date is defined as the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome.

Registration requirements apply to all new applicable clinical trials and ongoing trials that were initiated after September 27, 2007.

**How are applicable clinical trials registered?**
Clinical trials are registered via a web-based protocol registration system. Instructions for completing registration can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**What information must be provided to ClinicalTrials.gov?**
Detailed information about submission requirements can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). In general, initial registration must include administrative and contact information, start date, recruitment plans, location, and a lay person’s description of the study (e.g., purpose, study design, primary and secondary outcome measures, target number of subjects, etc.). Results of the study, information about adverse events, and a description of the quality assurance procedures used throughout the trial must also be provided in accordance with the time frames noted above.

**Who is responsible for registration?**
Responsibility for registration falls to the individual designated to be the “responsible party.” In many cases, the sponsor of the trial is the responsible party. However, the principal investigator is the responsible party in cases where there is no sponsor. Additionally, the sponsor can delegate all registration and reporting responsibilities to the principal investigator under the following conditions:

- The trial is initiated by the investigator,
- The investigator has access to and control over the data from the clinical trial, and
- The investigator has the right to publish the results of the clinical trial.

For research involving an IND (Investigational New Drug Application) or IDE (Investigational Device Exemption Application) with the FDA, the holder of the IND or IDE is the responsible party unless responsibility has been delegated to the principal investigator.

It is very important for researchers to know who the “responsible party” is, related to these requirements. Substantial penalties (i.e., monetary fines, withholding federal funds, denial of publication in an ICMJE journal, etc.) can be levied against responsible parties for failure to meet these requirements.

Principal investigators who are the responsible party may designate an individual to register the trial and complete registration information. However, it is ultimately the responsibility of the PI to ensure that registration occurs and the information provided is accurate and current.
How is registration handled for research projects conducted at multiple institutions?
The lead sponsor should take responsibility for registering the trial. In cases where there is no sponsor, investigators involved in the research must work with each other to identify a responsible party and ensure the trial is registered only once for the entire project.

How does registration of clinical trials relate to IRB review and approval?
IRB review is a separate process from clinical trial registration. IRB approval is not required prior to initial registration at ClinicalTrials.gov, nor does the IRB review any information submitted for registration. However, IRB approval is needed before research activity with human subjects is initiated (including recruitment of subjects).

Research participants must be informed of the availability of clinical trial information on ClinicalTrials.gov. Federal regulations require the following language to be included verbatim in informed consent documents for applicable clinical trials initiated on or after March 7, 2012:

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What are the consequences for failure to properly register an applicable clinical trial?
Under federal law, penalties for failure to register, or for providing incomplete, false, or misleading registration information (including updates subsequent to initial registration) may include civil monetary penalties of up to $10,000 per incident and/or per day, non-compliance notices from the FDA, and, for federally-funded trials, the withholding or recovery of grant funds. Additionally, unregistered or improperly registered trials risk not being accepted for consideration by ICMJE member or other journals.