

Guidance on Clinicaltrials.gov Registration

Which Johns Hopkins “clinical trials” must be registered?

As of January 25, 2008, the FDA requires that all new or ongoing trials* “that prospectively assign human participants or groups of humans to one or more health related interventions to evaluate the effects on health outcomes” must be registered at <http://www.clinicaltrials.gov>. “Health outcomes” include any biomedical or health-related measures, including pharmacokinetic measures and adverse events. Examples of such clinical trials include:

- Trials of Drugs/Biologics: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation. However, preliminary studies or Phase 1 trials to be published in an International Committee of Medical Journal Editors (ICMJE) journal should be included.
- Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric post-market surveillance.

Additionally, the revised requirements include provision of more data elements than under prior federal law, and these new requirements include:

- Primary and secondary outcome measures;
- Start date;
- Target number of subjects; and
- Adverse events.

For trials that are already registered, these new data fields as well as the previous data fields must be updated when there are changes to the study, or every 6 months, even if there are no changes.

(* An “ongoing” trial has enrolled one or more subjects and the final subject has not been examined or received an intervention for the purpose of collecting data on the primary outcome).

ICMJE Definition of “Clinical Trials”

The ICMJE policy on registration of clinical trials has been revised to broaden the definition of clinical trials to include preliminary studies or phase I studies (Clinical Trial Registration JAMA 298; 93-4, 2007). The ICMJE has adopted the World Health Organization’s definition of clinical trial as “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 outcomes include any biomedical or health-related measures including pharmacokinetic measures and adverse events. However, the ICMJE states “Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration.” The ICMJE’s *Frequently Asked Questions about Clinical Trials Registration* states, “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 policy applies to all trials that began enrollment on or after July 1, 2008.

Penalties for Failure to Register

Aside from the potential bar to publication of study results, there are now penalties for responsible parties who fail to register applicable FDA regulated clinical trials or who submit false or misleading information. Civil monetary penalties are allowed under FDA regulations. Civil penalties for investigator sponsors can range up to \$10,000/day (see, [Food and Drug Administration Amendments Act of 2007 \(FDAAA Law\)](#)). For federally-funded trials, the penalties could include withholding or recovery of grant funds.

Who should register a JHSPH clinical trial?

NIH guidance provides that the “responsible party” is either the sponsor of the study, 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 registration statute for the submission of clinical trial information. For more information about determining the “responsible party”, see:

<http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf>.

1. The sponsor of the clinical trial; OR
2. The Principal Investigator (PI)/sponsor of clinical trials that are investigator-initiated has the responsibility of:
 - a. Determining whether or not a trial for which he/she is the investigator/sponsor should be registered, AND
 - b. Completing and maintaining the information on the registration.

Note: Most NIH supported clinical trials expect the PIs to register the study but check with the NIH project officer.

Timing of Registration at ClinicalTrials.gov

For new clinical trials, submission requirements are triggered by enrollment. The PI or sponsor must submit required information no later than 21 days after the first participant is enrolled.

For ongoing clinical trials already registered, new information must be posted. A trial that was enrolling subjects as of September 27, 2007 (even one which does not involve a “serious or life-threatening disease or condition”) must be registered and updated at least annually (see details below).

What are the obligations of the JHSPH PI regarding registration if the trial is commercially sponsored?

The Johns Hopkins PI should consult with the commercial sponsor to ensure that posting the clinical trial on the government website is in accord with the terms of the study contract.

What are the requirements for updating clinical trial registrations?

1. Unless there have been no changes, registration information must be updated no less than once every 12 months.
2. If recruitment status for the study changes (ex., recruitment suspended), the registration must be updated within 30 days.
3. If the trial is complete (whether concluded or terminated prior to conclusion), registration must be updated within 30 days.

Requirements for posting basic study results:

The JHPSH faculty member who is the sponsor/investigator of a clinical trial is responsible for posting basic study results at the conclusion of the study. The following items must be posted on the site:

1. DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF PATIENT SAMPLE – A table of the demographic and baseline data collected overall and for each arm of the clinical trial to describe the patients who participated in the clinical trial, including the number of patients who dropped out of the clinical trial and the number of patients excluded from the analysis, if any.
2. PRIMARY AND SECONDARY OUTCOMES – The primary and secondary outcome measures, as stated in FDAAA Section 801, and a table of values for each of the primary and secondary outcome measures for each arm of the clinical trial, including the results of scientifically appropriate tests of the statistical significance of such outcome measures.
3. POINT OF CONTACT – A point of contact for scientific information about the clinical trial results.

Detailed instructions for submission of “Basic Results” may be obtained on the clinicaltrials.gov Protocol Registration System website at <http://prsinfo.clinicaltrials.gov/fdaaa.html>.

Additional Guidance and Resources

FDAAA Requirements for NIH Grantees At-A-Glance:

http://grants.nih.gov/ClinicalTrials_fdaaa/at-a-glance.htm

Definitions and Acronyms:

http://grants.nih.gov/ClinicalTrials_fdaaa/definitions.htm

Identifying an “Applicable Clinical Trial” under FDAAA:

http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf

PI Instructions on Submitting a Clinical Trial to clinicaltrials.gov

1. If you have not already done so, request a username and password from Miye Schakne, PRS Administrator, at mschakne@jhu.edu.
2. Go to the clinical trials.gov website to register your trial. <https://register.clinicaltrials.gov/>
3. Under Organization name, enter JHSPH. Then enter your username and password.
4. A clinical trial is registered in the ClinicalTrials.gov system by creating a "protocol record". Click on the "Create" link under Protocol Records on the Main Menu and fill in a series of data entry screens.

Data is saved as each screen is filled in, so that you can "Quit" at any time, saving the record for later completion using the "Modify" instructions provided below.

5. **Mark the protocol record as "Complete"** - After filling in the last data entry screen, the "Edit Protocol" screen appears with all of the information provided. Review the information for accuracy and completeness, and address "ERROR" messages, if any. "Alert" messages should also be addressed (and must be for trials that are not under U.S. FDA IND/IDE application).
6. **When the record is ready, click on the "Next Action: Complete" link near the top of the Edit Protocol screen.** Your PRS Administrator, Miye Schakne, will "approve" and "release" the record for publication on the ClinicalTrials.gov web site. The record should be available on the site within 2-5 business days of release by the administrator. If the record is not available within 10 days of completion, and you have not heard from the PRS quality assurance review personnel, please contact Miye Schakne at mschakne@jhu.edu.

Modify a protocol record - Once created, a protocol record can be modified at any time. Click on the "Modify" link under Protocol Records on the Main Menu. A selection list of all records owned by you appears, with status information for each record. Click on the "Edit" link next to the record that you wish to update. The Edit Protocol screen appears. Use the "Edit" links on the left to modify the desired portion(s) of the record.

When a record that is currently completed, approved or released is modified, the record status is automatically reset to "In progress". **Remember to mark the record as Complete when finished editing.** Your PRS Administrator will approve and release the modified record as described above.

7. **Keep protocol records up to date** – It is your responsibility to ensure that Protocol records for active trials are reviewed and modified as needed at least **every 6 months**. **Pay special attention to recruiting status and contact information**, as the accuracy and timeliness of this information is extremely important to potential participants in the research. Update the record's verification date (via the Edit Protocol screen) to confirm that the record has been reviewed.

Language to Include in consent documents

Clinical Trial Registration

You must insert the following language for any “applicable clinical trial”, see information at <http://prsinfo.clinicaltrials.gov/s801-fact-sheet.pdf>

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