



University of California
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Vice President—
Research & Graduate Studies

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LETTER Information

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CONTRACT AND GRANT OFFICERS

Subject: Registration of Clinical Trials – new Federal legislation and expanded ICMJE requirements

Background

In its implementation of the Drug Modernization Act (FDAMA) of 1997, the federal Food and Drug Administration (FDA) mandated that all clinical trials testing FDA-regulated drugs for efficacy in serious or life-threatening diseases or conditions must be registered on a publicly-available database. As a result, the website known as ClinicalTrials.gov, established and maintained by the National Institutes of Health (NIH), was created.

In 2005, the International Committee of Medical Journal Editors (ICMJE) began requiring registration of clinical trials that began subject recruitment on or after July 1, 2005 in public registries as a prerequisite for publication with a stated goal of promoting public good by making the existence and design of such trials publicly available. They defined a clinical trial as “Any research project 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.” An ‘intervention’ includes “drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like.” The policy specifically excluded registration requirements for FDA Phase I trials whose “primary goal is to assess major unknown toxicity or determine pharmacokinetics.” The eleven members of the ICMJE adopted this policy which required registration on one of a number of recommended public databases, including ClinicalTrials.gov. Many other non-member journals, including non-medical journals, have adopted ICMJE requirements, and the ICMJE maintains a [list of journals](#) that claim to adhere to its requirements.

New revisions to the FDAMA:

1) What trials to register?

In September 2007, the FDAMA was amended to expand the registration requirement for all “applicable clinical trials,” including Federal, industry-sponsored and investigator-initiated trials that are:

“1) Trials of Drugs or Biologics which are controlled clinical investigations, other than Phase I trials, of a product subject to FDA regulation and;

2) Trials of Devices which are controlled trials with health outcomes, other than small feasibility studies, and pediatric postmarketing studies.”

Additionally, the amended Act expands the scope of registration information that was previously optional, such as information regarding trial results or outcomes.

The FDAMA amendment also provides significant penalties for failing to register or for providing false or misleading information in connection with applicable trials and may include civil monetary penalties and, for trials that are federally funded, withholding or recovery of grant funds.

2) When to Register?

Trials initiated after September 27, 2007 or trials that are ongoing as of September 26, 2007 that do involve a “serious or life-threatening disease or condition” must be registered in full by the later of September 26, 2007 or 21 days after the first subject is enrolled.

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

Trials that were ongoing as of September 27, 2007 that do involve a “serious or life-threatening disease or condition” and were completed by September 26, 2007 are not subject to this requirement, though may be subject to pre-existing registration requirements.

3) Who Must Register?

The “responsible party” who must register the trial is defined by statute as either:

- the sponsor of the clinical trial as defined in 21 CFR 50.3; i.e. the holder of an IND or IDE
- the principal investigator if s/he is so designated by the sponsor

4) Application and Progress Report Requirements for NIH-Funded Grants

Competing (new and renewal) applications submitted on or after 1/15/08 and non-competing progress reports with budget start dates on or after 4/1/08 that include clinical trials must be registered with ClinicalTrials.gov and include basic trial registration data. If a new applicable trial is proposed in a competing application, the research plan should include a statement that the application includes a trial that requires registration in ClinicalTrials.gov.

Expanded requirements by ICMJE:

Also in 2007, the ICMJE expanded the scope of trials to be publicly registered to include “any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes.” Specifically, this now includes Phase I clinical trials.

Presently, the ICMJE follows the 2005 guidelines and does not enforce the inclusion of Phase I trials, however, trials where enrollment begins on or after July 1, 2008 will need to comply with the ICMJE’s 2007 requirements in order to have publications accepted by member journals.

Summary

While the FDAMA requirements are narrower than what will soon be required by the ICMJE, particularly concerning the issue of Phase I trials, the ICMJE encourages researchers to err on the side of more broad registration to ensure manuscripts will meet standards of acceptability. Additional information can be found on the ICMJE's Frequently Asked Questions document located at: <http://www.icmje.org/faq.pdf>.

With respect to the expanded scope of information that the FDAMA will eventually require be listed on ClinicalTrials.gov, such as trial results, we hope to have an opportunity to submit comments as part of any rulemaking process by the FDA, and in advance of expansion of data fields on the website. Once the FDA issues further guidance, RAO will issue additional guidance to campuses.

Please refer to the following links for additional guidance and FAQs:

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-023.html>

http://grants.nih.gov/grants/policy/hs/faqs_aps_clinical_trials.htm

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