Clinical Trial Registration

As many of you know, all investigators who perform a clinical trial (as defined herein) must now by law ensure that the trial is registered on a government web site called *ClinicalTrials.gov (CT.gov)*. This communication is being distributed to clarify the requirements for registration and to provide guidance on how to register ongoing trial(s) or ensure that future trials are registered prior to being initiated.

Background:
On December 20, 2007, we were notified of new FDA requirements for the registration of clinical trials (Public Law 110-85). The new law expands the scope of trials that must be registered and defines the responsibilities of the principal investigator with respect to trial registration. In addition to the requirement described by the FDA, the International Committee of Medical Journal Editors (ICMJE) also mandates registration of clinical trials prior to accepting any manuscript for publication in any of their member biomedical journals. While both organizations require registration, there has been some confusion about what constitutes a clinical trial and which trials require registration, particularly since each organization has a different definition.

Definition of Clinical Trial:
The FDA requires registration for "applicable clinical trials" defined as follows:

- For any trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.
- For trials of biomedical devices: controlled trials with heath outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.

ICMJE adopted a broader definition of a clinical trial, consistent with the definition developed by the WHO. The ICMJE definition includes:

- 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.

Beginning in July 2008, it will be mandatory to register *all* clinical trials, including phase 1 and pharmacokinetic trials, if you intend to publish a study in one of the biomedical journals under the auspices of ICMJE.

> *Because of the differing registration requirements between the FDA and ICMJE, we strongly recommend that all clinical trials be registered, except those that involve retrospective review of clinical data and/or are purely observational studies that do not involve any intervention or randomization.*

Who Is Responsible for Registering a Clinical Trial?
By law, the "responsible party" must register a clinical trial. The responsible party is defined as:

- The sponsor of the clinical trial

or

- The principle investigator (PI) of the clinical trial if so designated by a sponsor, grantee, contractor, or awardee. For most clinical trials, the PI should register the trial, since it is the PI who is responsible for conducting the trial, has access to and control over the data, has the right to publish the results of the trial, and has all of the information necessary to complete the registration.
- For those studies that involve an application for an Investigational New Drug (IND) or Investigational Device Exemption (IDE), the responsible party may be someone other than the PI. However, if you receive NIH or other government funding for a trial, particularly those that do not include an IND or IDE application, the PI is the responsible party. To ensure that any extramurally funded trial is properly registered, you should contact the sponsor for clarification.
- For clinical trials that are being performed at multiple institutions, the lead sponsor should take responsibility for registering the trial. If you are not the PI or lead sponsor, you should work with the other investigators and sponsors to ensure that the trial is registered only once for the entire project.

How Do I Register a Clinical Trial?
Clinical trials are registered with *CT.gov* via a web based data entry system called the Protocol Registration System (PRS). Prior to registering the trial, you must obtain a user account which will be required to login to the PRS and register your trial. If you attempt to register directly, the site will redirect you to a local administrator to obtain a user account.

At UCSF, the Industry Contracts Division of the Office of Sponsored Research can setup a user account for you. To obtain an account and register a trial please follow the detailed instructions on the last page of this memo.

If your primary appointment is at an affiliate institution that is using the services of the UCSF Human Research Protection Program (HRPP), please contact your affiliate administrative office to determine who is serving as an administrator for protocol registration.

When Should I Register My Clinical Trial?
You should register a trial before any subjects are enrolled. The FDA requires you to register no later than 21 days after the first subject is enrolled; however, the ICMJE requires registration before the first subject is enrolled. To avoid publication restrictions imposed by the ICMJE, register your trial before enrolling the first subject.

Since you can register your trial prior to receiving IRB (Committee on Human Research [CHR]) approval, you are encouraged to register as early as possible to avoid any potential conflicts between enrolling subjects and ICMJE or FDA regulations. As part of the process at UCSF for receiving CHR approval, the CHR will request the *CT.gov* registry number (called an "NCT number") for your trial.

Even if No Changes Have Been Made to a Previously Registered Trial, Do I have to Update the Registration of that Trial?
Yes. The FDA and ICMJE require that trial registrations are reviewed and affirmatively verified even if no changes have been made to the trial. To verify a trial please follow the detailed instructions on the last page of this memo.

If Changes Have Been Made to a Previously Registered Trial, When Do I have to Update the Registration of that Trial?
The FDA and ICMJE require that trial registrations are updated within 30 days of a change to the trial. To update a trial please follow the detailed instructions on the last page of this memo.

Who Do I Contact with Questions about the Registration of a Clinical Trial?
If you have any questions regarding registration of a clinical trial, please contact PRS directly at register@clinicaltrials.gov.

You may also contact the Industry Contracts Division of the Office of Sponsored Research at UCSF at industrycontracts@ucsf.edu.

Steps to Registering Your Clinical Trial on *ClinicalTrials.gov*

Clinical trials are registered on *ClinicalTrials.gov* (*CT.gov*) via a web based data entry system called the Protocol Registration System (PRS). ***As a PRS user, you are responsible for ensuring that the information you provide on your trial is correct, complete, readily understood by the public, and updated in a timely manner.***

Before you begin, please ensure that you are responsible for registering the trial. In general, UCSF investigators should only register investigator-initiated trials where they are the principal investigator.

1. Obtain a User Account: To obtain a PRS user account, send an email to industrycontracts@ucsf.edu with "Request for CT.gov User Account" in the subject line and your name, email address, and department in the body of the message. A representative of the Industry Contracts Division of the Office of Sponsored Research at UCSF will setup a user account for you, and you will receive an email from *CT.gov* containing the information that you will need to login.

2. Login to PRS: Go to http://register.clinicaltrials.gov and enter the login information that you received from *CT.gov*. The first time that you login to the PRS you will need change your password using the "Change password" link under "User Account" on the Main Menu.

3. Create a Protocol Record: A trial is registered in the *CT.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.

4. Review the Protocol Record: After filling in the last data entry screen, the "Edit Protocol" screen will appear. Review the information that you entered for accuracy and completeness, and address any *ERRORS*, *ALERTS*, *WARNINGS*, or *NOTES* in the protocol record. If you fail to address any *ERRORS* or *ALERTS* you can not complete the registration process. *ALERTS* and *WARNINGS* may indicate that required information is missing.

5. Mark the Protocol Record as Complete: After you have reviewed the protocol record and corrected or addressed all *ERRORS, ALERTS, WARNINGS and NOTES*, you must click on the "Next Action: Complete" link near the top of the Edit Protocol screen. If you fail to mark your record as "Complete" it will not be approved and released for publication on *CT.gov* and your trial will not be properly registered.

6. Keep Your Protocol Record Up-to-Date: An affirmative verification or update of the data in protocol records that have not been closed or terminated is required every 6 months. Failing to login to the PRS and confirm or update your record(s) every 6 months, regardless of whether there has been a change to the trial or not, may result in a loss of funding and/or the inability to publish the results of a trial in an ICMJE associated journal.

To update your protocol record, login to the PRS and click the "Modify" link on the Main Menu. Click "Edit" next to the record to be modified and then "Edit" next to the field(s) to be modified. If no changes are required, you must still update the "Record Verification Date" field with the current date. Make sure to click "OK" to save the changes, and mark the record as "Complete." If you fail to mark your record as "Complete" it will not be approved and released for publication on *CT.gov* and your trial will not be properly registered.

IMPORTANT NOTE: Acceptance by PRS and assignment of an NCT number to a protocol record does not ensure compliance. When registering your trial, you must ensure that the information provided is accurate and complete, and that you login to the PRS on a regular basis to review and update your record. Failing to follow all requirements defined herein may result in a loss of funding and/or the inability to publish the results of a trial in an ICMJE associated journal.

For additional information, *please login to the PRS and refer to the PRS User's Guide and Data Element Definitions.*

For questions, *please contact CT.gov at register@clinicaltrials.gov. You may also contact the Industry Contracts Division of the Office of Sponsored Research at UCSF at industrycontracts@ucsf.edu.*