ClinicalTrials.gov

REGISTRATION REQUIREMENTS

Background: *What is it?*

- ClinicalTrials.gov is a public registry that provides easy access to information on clinical studies, both clinical trials and observational studies that are unfunded or funded by Federal agencies, pharmaceutical companies, academic medical centers, voluntary groups, and other organizations.
- Information is provided and updated by the sponsor or principal investigator.
- The website is maintained by the U.S. National Library of Medicine at the National Institutes of Health (NIH).

CT.gov Clinical Studies

- **Clinical Trial –** participants receive specific interventions according to a research plan or protocol created by investigators. Interventions may be medical products, such as drug or devices; procedures; or changes to participant's behavior.

- **Observational Studies –** investigators assess health outcomes in groups of participants according to a protocol or research plan. Participants may receive the above interventions, or procedures as part of their routine medical care, however are not assigned specific interventions by the investigator.

Study Record Information

- Each summary of a study protocol contains:
  - Disease or condition
  - Intervention
  - Title, description, and design of the study
  - Locations where the study is being conducted
  - Contact information for study locations
  - Links to relevant information on other health websites
- Some records include:
  - Description of study participants
  - Outcomes of the study
  - Summary of adverse events experienced by study participants

Purpose: *Why register?*

- Requirement by U.S. Food and Drug Administration laws
- Certification for U.S. Department of Health & Human Services (DHHS) grant applications and progress reports
- Publication of research studies that assigns human subjects to health-related intervention and evaluates their outcomes
- Reimbursement for Medicare / Medi-Cal claims for items and services in clinical trials qualified for coverage

Noncompliance may result in:

- Civil monetary penalties (up to $10,000 per day)
- Withholding / recovery of federal funds
- Withholding of publications

Requiring Agencies

U.S. Department of Health and Human Services (DHHS)

- Food and Drug Administration (FDA)
  - Modernization Act of 1997 (FDAMA)
  - FDA Amendments Act of 2007 (FDAAA)
- U.S. Department of Health and Human Services (DHHS), National Institutes of Health (NIH) and other grant agencies
- Center for Medicare & Medicaid Services (CMS)

Publication Purposes

- International Committee of Medical Journal Editors (ICMJE)
- World Health Organizations (WHO)
- World Medical Association (WMA) General Assembly
  - Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects

Responsible Party

- **Sponsor:** Primary organization that oversees implementation of study and is responsible for data analysis.
- **Responsible Party:** Either (1) the ***Sponsor*** of the clinical trial, or (2) the ***Principal Investigator*** of the clinical trial designated by a sponsor, grantee, contractor, or awardee.

  (3) ***Sponsor-Investigator***: the individual who both initiates and conducts the study

When to Register

- Federal agencies require registration of applicable clinical trials **21 days after the first study subject enrollment**.

- Publication requirements recommend registration **prior to any human subject enrollment.**

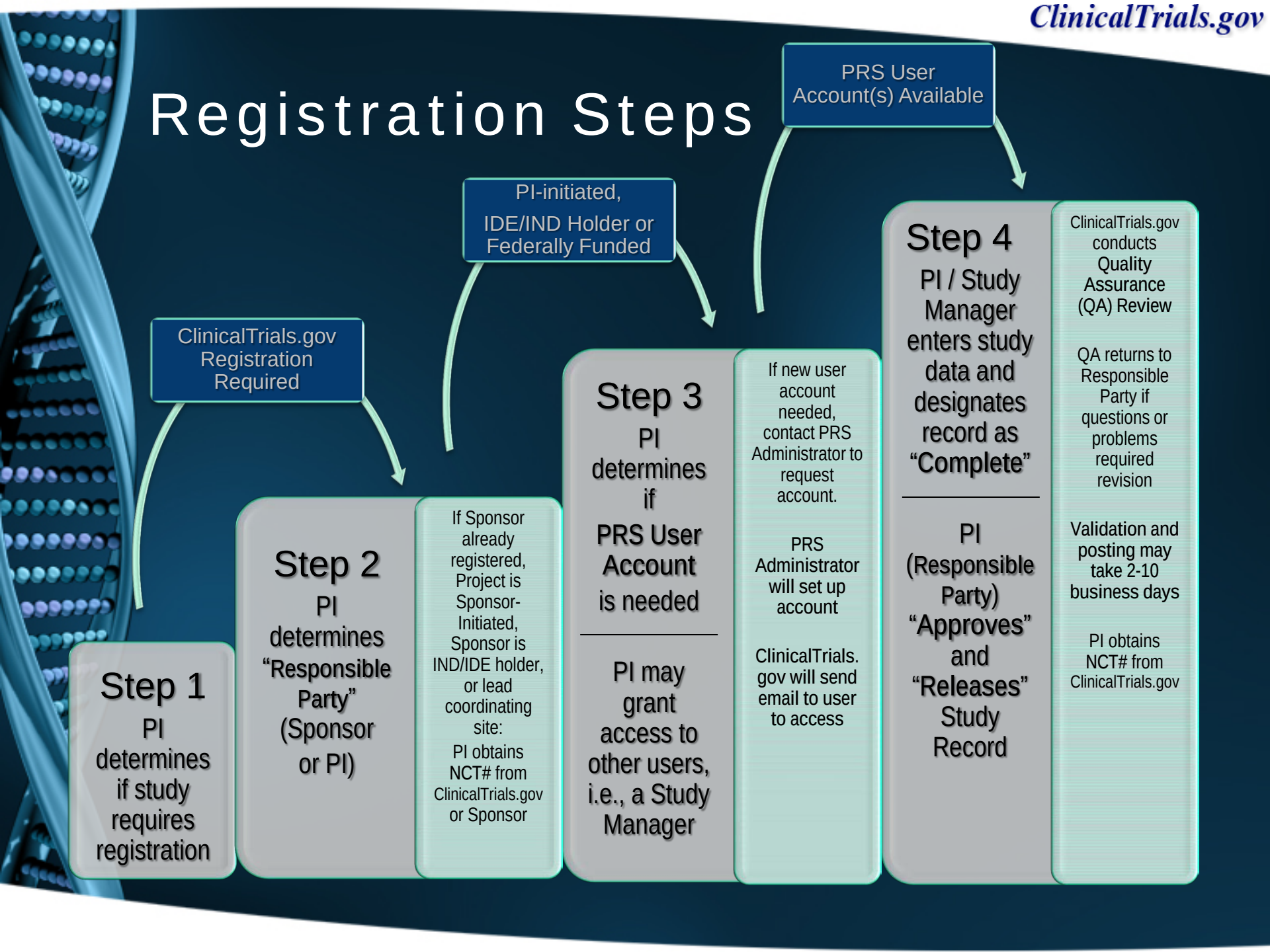
Required Updates

- Responsible Parties should update records **within 30 days** of a change to :
  - **Recruitment Status**
  - **Completion Date**
- **Other Changes**, such as **protocol amendments** should be completed at least every **12 months**
- It is recommended that **Record Verification Date** be updated at least every **6 months**

Report Results

- Results of an Applicable Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be submitted by the Responsible Party **no later than 12 months after the Completion Date**.
  - Extensions may be granted for up to two years with certification
- Voluntary or only publication registrations do not require submission of results.

Registration Steps



Reasons to Register

1) Study is a clinical trial that uses a drug or device
2) A DHHS grant application or progress report is being prepared for a clinical trial
3) A federal reimbursement claim is being prepared for items and services under a clinical trial
4) Study involves assignment of a health-related intervention to evaluate the effects on health outcomes and will be published

FDA Registration Requirements

Applicable Clinical Trial (ACT) defined by Section 801 of the Food and Drug Administration (FDA) Amendments Act must be registered within twenty-one (21) days after first enrollment.

1. Initiated after September 27, 2007, or initiated on or before that date and is still ongoing as of December 26, 2007;
2. Trials of drug biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs biological products subject to FDA regulations;
3. Trials of devices: (1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and (2) pediatric post-market surveillance required by FDA

DHHS Registration Requirements

- **DHHS Applications and Progress Reports**

  Signature by an Authorized Organizational Representative (Signing Official) at the time of submission must certify FDAAA compliance in applications and progress reports for applicable clinical trials

- NIH encourages registration and results reporting for all NIH-supported clinical trials, regardless of whether or not they are subject to FDAAA

  NIH Clinical Trial Definition NOT-OD-15-015

  For competing applications due on or after January 25, 2015

  A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

NIH Current Implementation

For Competing and Non-Competing Applications

Human Subjects section of the Research Plan must include a heading entitled “ClinicalTrials.gov”

Clear statement should be provided for either:

- Project includes an applicable clinical trial which will require registration in ClinicalTrials.gov.

- OR-

- ClinicalTrials.gov registry number (which is “NCT” followed by an 8-digit number, e.g. NCT00000418),
- Brief Title (protocol title intended for the lay public),
- Responsible Party Contact Information (name, organization, e-mail address)

CMS Registration Requirement

- **Center for Medicare and Medicaid Services (CMS) Billing Invoices**

  An 8-Digit ClinicalTrials.gov Number is required on all claims for items and services provided in clinical trials that are qualified for coverage as specified in the Medicare National Coverage Determination Manual, as of January 1, 2014

ICMJE Registration Requirements

International Committee of Medical Journal Editors (ICMJE) Clinical Trials Registration Policy

- ICMJE requires trial registration as a condition for publication of research results generated by a clinical trial at or before the time the first patient enrollment after July 1, 2005
- ICMJE Clinical Trials Definition: 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
- In addition to ClinicalTrials.gov, ICMJE accepts registration in other acceptable registries that participate in the World Health Organization (WHO) International Clinical Trials Portal (ICTP)

Responsible Party

University of Southern California (USC) will delegate to the PI as Responsible Party for registration when:

- USC is prime grantee on a federal grant funded study;
- Study is unfunded and does not involve any drugs or devices; or
- Study is investigator-initiated

Registration should be handled by company, contract research organization, or other party when:

- USC is part of a multi-site project;
- Company holds Investigational Device Exemption IDE) or Investigational New Drug (IND)
- USC should obtain the ClinicalTrials.gov number from the registering organization

Responsible Party Delegation

Before accepting the role a Responsible Party,
USC Principal Investigator (PI) should ensure he/she is:

(1) responsible for conducting the trial,

(2) has access to and control over the data from the clinical trial,

(3) has the right to publish the results of the trial, and

(4) has the ability to meet all of the requirements for the submission of clinical trial information.

Protocol Registration & Results System (PRS)

USER ACCOUNTS are created by assigned PRS Administrator(s) for the institution

The Principal Investigator will serve as the:

1) **Responsible Party** to Approve and Release the Study Record; and

2) **Record Owner** to add Other Users to the Access List to enter study data, edit/update, and enter results

Additional contacts may be entered by location

PRS Administrators for User Accounts

Send an email to the PRS Administrator to request a PRS User Account:

- Cancer Center Studies

  Kay Johnson, R.N., Associate Director

  Johnson_K@med.usc.edu

  (323) 865-0457

- Non-Cancer Studies & All Other Requests

  Jean Chan, Associate Director

  jeanbcha@usc.edu

  (323) 442-2825

ClinicalTrials.gov Number

- The PI or Study Manager will enter all information and designate the record as **COMPLETE**
- The PI/Responsible Party will **APPROVE** and **RELEASE** the Study Record
- Errors or questions will be returned to the PI for revision and resubmission
- A ClinicalTrials.gov Number will be issued within 2-10 business days after a Quality Assurance Review is conducted.