


ClinicalTrials.gov

Registration and Results
Reporting on ClinicalTrials.gov

Marlene Berro, MS, RAC (UCSF)
Denise Owensby, B.S., C.C.R.P. (UCD)



2

ClinicalTrials.gov

- Operated by the National Library of Medicine (NLM)
- Most Academic Medical Health Centers have institutional accounts
 - Individual investigators/employees are given user profiles on that account
- Each study gets only one record, regardless of number of sites
- Each study should be registered by the Responsible Party (RP)
- Each institutional account can have many records/studies
 - Each user can access multiple records/studies under his/her profile
 - While users can edit such records, only the RP can release it
- Type of information in ClinicalTrials.gov
 - Registration
 - Results
 - Adverse Events

Evolution of Clinical Trial Disclosure Requirements

- 1997: FDAMA establishes ClinicalTrials.gov
- 2000: ClinicalTrials.gov launched
- 2005: ICMJE requires registration of trials (including at ClinicalTrials.gov)
- 2007: FDAAA expands ClinicalTrials.gov to require registration of more studies and results and adds penalties for noncompliance
- 2008: ClinicalTrials.gov adds basic results modules, including adverse events

Source: <http://clinicaltrials.gov/ct2/about-site/history>

4

Rationale



- Increase research transparency
- Help people find trials

To learn more, visit: <http://clinicaltrials.gov/ct2/manage-recs/background>

5

Why Register? It's the law!



FDA Amendments Act of 2007 (FDAAA)

Most prospective clinical trials involving regulated drugs, biological products, and devices must be registered on ClinicalTrials.gov. (The law also requires reporting of results and adverse events for a subset of these studies.)

To learn more about FDAAA 801 Requirements, visit: <http://clinicaltrials.gov/ct2/manage-recs/fdaaa>

6

FDAAA - Registration

Required for "Applicable Clinical Trials":

- Interventional studies (drugs, biologics, devices)
- Phase 2 – 4 (not phase 1 drug; not small feasibility device;)
- US FDA jurisdiction (e.g., IND/IDE or US site)
- Studies initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007

When:

- Within 21 days of enrollment of 1st subject
- Update at least every 12 months (30 days for Recruitment Status and Primary Completion Date)

<http://clinicaltrials.gov/ct2/manage-recs/fdaaa>

7

ClinicalTrials.gov – Registration Information

- Description of study
 - Study type, Phase, Design, Outcome measures
- Recruitment information
 - Eligibility criteria, locations, recruitment status
- Administrative and other information
 - Key dates and contact information
- Helpful links to add
 - MEDLINE publications, consumer health information, FDA information

8

ICMJE - Registration

- When to register:
 - **Prior to enrollment of 1st subject**
- ICMJE doesn't require results submission
- ICMJE will not consider results data posted in the tabular format required by ClinicalTrials.gov to be prior publication

Source: http://www.icmje.org/publishing_10register.html

9

ICMJE – Registration: Which studies?

Required for Prospective studies that:

- Assign subjects to an intervention or concurrent comparison or control groups
- Study the cause/effect relationship between medical intervention and a health outcome.

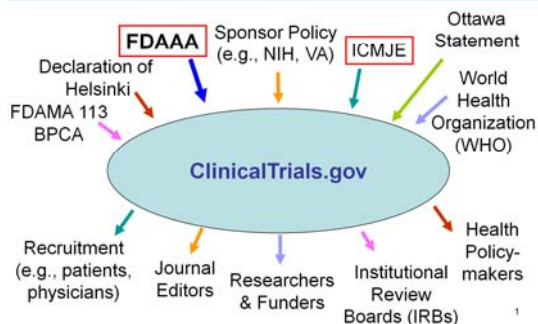
ICMJE scope is much broader than the scope of FDAAA:

- *Interventions* include **procedures, behavioral treatments, dietary interventions**
- *Health outcomes* include any biomedical or health-related measure obtained in participants, including **pharmacokinetic measures** and adverse events

Source: http://www.icmje.org/publishing_10register.html

10

Policies and Users



Updated from D. Zarin, ClinicalTrials.gov, *Overview of ClinicalTrials.gov presentation*, December 2008, http://prsinfo.clinicaltrials.gov/webinars/module1/resources/Overview_Handouts.pdf.¹¹

1

Who is responsible for registering the trial?

ICMJE:

Anyone can register, but the author is responsible for ensuring complete registration

FDAAA:

The **Responsible Party (RP)** defined as...

- The Sponsor (or Sponsor-Investigator):
 - IND/IDE holder
 - If no IND/IDE, the industry, academic institution or other organization that initiated the study

12

Who is the Responsible Party?

1. Department funded/ PI initiated research
2. NIH funded research/ "Your U" is the grantee institution
3. Pharmaceutical company funded research/ multi-center study including site at "Your U"
4. Device company funded research/ "Your U" PI is the IDE holder
5. Cooperative Group study

13

Responsible Party versus Owner

Anyone can be the owner of a study. Owners are often Study Coordinators or study team members, and assist the Responsible Party with data entry.

The Responsible Party (RP) is **legally** responsible for registering their study record on ClinicalTrials.gov, ensuring accuracy, and making sure that the content is up-to-date. An RP must "Approve" and "Release" a study record onto ClinicalTrials.gov.

- Identification of RP
 - Sponsor – Organization that initiates the study or
 - Principal Investigator (PI) –Only if designated as the RP by the Sponsor Organization or
 - Sponsor-Investigator – Individual who both initiates and conducts

Owners and RP must be Protocol Registration System (PRS) users of the organizational account.

14

FDAAA: Designation of Responsible Party

RP can be designated by the Sponsor to a PI who:

- Is responsible for conducting the study
- Has access to and control over the data
- Has the right to publish the trial results, AND
- Has the ability to meet the requirements

Example of RP designation

- PI initiated study at "Your U" funded by NHLBI
 - "Your U" is the Sponsor (grant funding recipient)
 - "Your U" can be the RP or designate the PI as the RP
 - Note: even if not designated as RP, the PI can still enter data into ClinicalTrials.gov

15

Responsibilities of an Owner of Study Records on ClinicalTrials.gov.....

- You are responsible for maintaining the study records associated with your account.
- When you enter information about the study, please ensure the information is correct, readily understood by the public, and updated in a timely manner.
- Only one owner can be assigned to a study record, but the owner can also allow other users to edit the study record. Use the Access List.

[In Progress](#) | [Completed](#) | [Approved](#) | [Released](#) | [Upload: Allowed](#) [[Set...](#)]
 Owned by: [MNorton](#) [Access List](#) Last updated: 07/25/2012 16:11 by MNorton
 Initial release: [not yet released]

16

Ongoing Responsibilities of an Owner of Study Records on ClinicalTrials.gov.....

- Records can be transferred to other user accounts as staff change.
- Records must be updated every 6 months – unless Overall Recruitment Status changes, then you should update the record within 30 days.

Record Verification Date: * [FDAAA](#) July Year: 2012

- Records must be updated within 30 days after the completion date.
- Failure to update information on ClinicalTrials.gov can result in penalties

Study #1

Effectiveness of Bupropion for Treating Nicotine Dependence in Young People

- Study Design: Multi-center, Randomized, Efficacy Study
- Interventions: Bupropion, Placebo
- Primary Outcome: Smoking behavior over 6 months

Register? For FDAAA? For ICMJE?
 Results?
 Responsible Party?

18

Study #2

Effects of Chronic Sleep Restriction in Young and Older People

- Study Design: Open label, Crossover Assignment
- Interventions: Chronic sleep restriction
- Primary Outcome: Changes in sleep and waking EEG measures, frequent measures of performance, attention, alertness
- Other fact: Two universities collaborating, Dr. A @ AU and Dr. B at BU; Dr. B designed study, but A will enroll more

Register? For FDAAA? For ICMJE?

Results?

Responsible Party?

19

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

ClinicalTrials.gov can be searched in real time to find enrolling and completed studies including

- Conditions
- Interventions
- Outcome measures
- Sponsors/collaborators
- Locations
- Phases
- Dates (Start and Completion)
- Results

20

<http://www.ClinicalTrials.gov>

The screenshot shows the ClinicalTrials.gov homepage. At the top, it says "ClinicalTrials.gov" and "A service of the U.S. National Institutes of Health". Below this, it states "ClinicalTrials.gov currently lists 138,000 studies with locations in all 50 states and in 152 countries." The main content area is divided into several sections: "Search for Studies" with a search bar and "Advanced Search" link; "Search Help" with links for "How to search", "How to find results of studies", and "How to read a study record"; "Locations of Recruiting Studies" with a pie chart showing the distribution of studies by location (Non-U.S. Only: 46%, U.S. Only: 45%, Both U.S. & Non-U.S.: 9%); "For Patients & Families", "For Researchers", and "For Study Record Managers" with various links and resources; and "Learn More" with links for "New Site and New Content for ClinicalTrials.gov" and "Glossary of common site terms". At the bottom, there are navigation links for "HOME", "RSS FEEDS", "SITE MAP", "TERMS AND CONDITIONS", "DISCLAIMER", and "CONTACT NLM HELP DESK".

21

Recent News



- Two New Optional Data Elements for AHRQ Registry of Patient Registries
- Responsible Party, Primary Completion Date, and at least one Primary Outcome Measure will be needed to release a new study record beginning on December 1, 2012

22

Help for Registering Studies on ClinicalTrials.gov

- “Submit Studies” at <http://clinicaltrials.gov/ct2/manage-recs>
- “For Researchers” at <http://clinicaltrials.gov/ct2/help/for-researcher>
- “For Study Record Managers” at <http://clinicaltrials.gov/ct2/help/for-manager>

23

FDAAA – Results Submission

Required for:

- Applicable Clinical Trials
- In which the study product is approved (*for any use*) by FDA

When:

- Within 12 months of Primary Completion Date (final data collection for primary endpoint)
- If product not approved by Primary Completion Date but is approved later, then results due 30 days after approval
- Delays are possible, primarily for manufacturer or under limited special circumstances
 - Pending publication is NOT considered a good cause for delay

<http://clinicaltrials.gov/ct2/manage-recs/fdaaa>

24

Informed Consent Language

- **FDA Mandated Changes in Consent Form Language**
- The FDA has added a new element of consent that is required for “applicable clinical trials.” All applicable clinical trials are required to include this new element of consent by March 7, 2012.
- By federal regulation, the required language must be incorporated verbatim and **cannot be altered in any way**. “A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by US 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.**”
- Subjects who were consented before March 7, 2012 will NOT have to be re-consented or otherwise sign addendum consent with this language. For more information or questions, contact the “YOUR U” IRB office or office of regulatory affairs.

25



26

Consequences of Noncompliance

FDAAA

- Public notices of noncompliance and violations
- Withholding of NIH funds
- FDA sanctions
- Civil monetary penalties (up to \$10,000/day)

ICMJE

- Cannot publish in journals following ICMJE policy, and other select journals



27

Publications

International Committee of Medical Journal Editors (ICMJE)

- Requires registration in a publicly available, searchable system.
- Scope is broader than FDAAA (i.e., all clinical trials).
- Includes 1000+ journals that have adopted the ICMJE policy, such as BMJ, JAMA, and NEJM. Source: <http://www.icmje.org/journals.html>

28

UCSF Case Study

Dear Dr. XXXXXXXX, Thank you very much for submitting your manuscript above for review by PLOS ONE. After careful consideration, I regret we have decided that your manuscript does not meet our criteria and is therefore not suitable for publication in PLOS ONE. The PLOS journal policies regarding trial registration have become stricter over time and we now only consider studies for review that were registered before patient recruitment began. Specifically, our policy states that "trials initiated after 1 July 2005 must be registered prospectively in a publicly accessible registry (i.e., before patient recruitment has begun), or they will not be considered for publication." As this study began in January 2006 and was registered February 17, 2009, unfortunately we cannot consider it further. I am sorry that we cannot be more positive on this occasion, but hope that you appreciate the reasons for this decision. Yours sincerely, Lindsay Morton, Publications Assistant, PLOS ONE On behalf of Matt

29

Challenges for compliance

- Issues contributing to challenges for compliance with Federal Regulations for registering studies in ClinicalTrials.gov

30

How to identify which studies need to be registered?

- Does site have plan/SOP/mechanism to identify the studies required to be registered?
 - According to FDAAA?
 - According to ICMJE?

- Current approaches:
 - UCSF
 - UC Davis

31

Who and Where are the campus CT.gov PRS Administrators?

- Where should it be housed for UCs?
- Should this be the same for all UC campuses?
- Which department?
 - Compliance?
 - IRB?
 - Clinical Trials Office (CTSC)?
 - Office of Research?

32

ClinicalTrials.gov

University of California Account Information

Campus	CT.Gov Account Type	Total Records/	CT.Gov Admin Department
Davis	Institutional	238 Records	Clinical and Translational Science Center (CTSC)
Irvine	Institutional	N/A	Clinical Trials/Research Support Services Office of Research
Los Angeles	1. PI Accounts 2. Cancer Center has central account	N/A	1. PI 2. Cancer Center
San Diego	PI Accounts	N/A	N/A
San Francisco	Institutional	750 Records	Office of Ethics and Compliance Office of Research

33

Designation of Responsible Party

- For Federal grant studies – Institution is grantee
- How is this delegated to PI?
 - Only the Responsible Party can Approve & Release any/all updates to CT.gov listing

34

Educating Principal Investigators

Regulations and Registration Responsibilities?

- Website Instructions
- Educational workshops
- Individual training
- Letter from Compliance
- (Generally trainings only attended by study coordinators or other regulatory staff)

35

Registration Compliance

- Initial entry into registry
- Updates per federal regulation requirements
- Results reporting

36

Basic Results Reporting

- Difficult
- Time Consuming
- Generates Errors as soon as started for all non-filled required elements

37

Administration of CT.gov

- FTE Required
- Time required for follow-up on all reporting requirements
- Numbers of study listings to manage
- Funding
- Again...Which department/office???

38

This slide set was adapted from a collaboration of CTSA organizations (Mayo Clinic, Partners, University of Michigan Medical School, University of Rochester) and the National Library of Medicine.

The Clinical and Translational Science Awards Program (CTSA) is part of the Roadmap Initiative, Re-Engineering the Clinical Research Enterprise and is funded by the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH).

39

For More Information please contact:

Marlene Berro
UCSF Office of Ethics
and Compliance
415.476.9429
marlene.berro@ucsf.edu

Denise M. Owensby
Clinical and Translational
Science Center
UC Davis Health System
916.703.9191
denise.owensby@ucdmc.ucdavis.edu
