ClinicalTrials.gov

Why Does it Affect Me? Should I Be Concerned?

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This slide set was made possible by a collaboration of CTSA Organizations
Be aware that...

- Any PowerPoint presentation can only be an introduction to a topic.
- This subject is complex – this will point you to many other resources – and our office is happy to assist you further.
- PowerPoint bullets are neither the law nor the regulations that apply.
Learning Objectives

- Explain what ClinicalTrials.gov is and what it can do
- Explain why you should register your study
  - FDAAA
  - ICMJE
  - Voluntary (Recruitment etc.)
- Identify who is responsible for registration
- Provide practice examples
- Explain how registration works at Ohio State University, College of Medicine
- Help Resources (institutional & national)
What is ClinicalTrials.gov?

Why should I be concerned?
http://www.ClinicalTrials.gov

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more about clinical studies and about this site, including relevant history, policies, and laws.

ClinicalTrials.gov currently lists 133,291 studies with locations in all 50 states and in 179 countries.

Search for Studies
Example: "Heart attack" AND "Los Angeles"

Search Help
- How to search
- How to find results of studies
- How to read a study record

For Patients & Families
- How to find studies
- See studies by topic
- Learn about clinical studies
- Learn more...

For Researchers
- How to submit studies
- Download content for analysis
- About the results database
- Learn more...

For Study Record Managers
- Why register?
- How to register study records
- FDAAA 801 Requirements
- Learn more...

Locations of Recruiting Studies
- Non-U.S. Only (49%)
- U.S. Only (45%)
- Both U.S. & Non-U.S. (7%)

Total N = 28,980 studies
Data as of September 27, 2012

Learn More
- New Style and New Content for ClinicalTrials.gov
- Glossary of common site terms
- For the Press
- Using our RSS Feeds

Copyright | Privacy | Accessibility | Viewers & Players | Freedom of Information Act | USA.gov

Wexner Medical Center
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
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
Rationale

• Increase research transparency

• Help people find trials

To learn more, visit: http://clinicaltrials.gov/ct2/manage-recs/background
Value of Transparency

- Public knows how its money is being spent;
- Quicker and wider public access than some publications provide;
- Suppression of research results impedes the scientific process in all areas of science;
- Trials Results inform the public’s medical decisions;
- Unacknowledged changes are made to the trial protocol that would affect the interpretation of findings;
- Publications do not always include all prespecified outcome measures;
- Provide a place where researchers can see what is going on elsewhere – even before results exist, to avoid duplication of effort.
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
Recent News

- August 18, 2011 ClinicalTrials.gov changes requirements for study release. The Responsible Party (Principle Investigator) for most Investigator Initiated studies has the sole authority to release records.
- March 7, 2012 Informed Consent Language mandated by FDA For Applicable clinical trials.
- TEST ACT 2012 in process expanded regulations for reporting.
Policies and Users

- FDAAA
- Declaration of Helsinki
- FDAMA 113
- BPCA
- Sponsor Policy (e.g., NIH, VA)
- ICMJE

ClinicalTrials.gov

- Ottawa Statement
- World Health Organization (WHO)
- Health Policy-makers
- Institutional Review Boards (IRBs)
- Researchers & Funders
- Journal Editors
- Recruitment (e.g., patients, physicians)

Why should I register a trial in ClinicalTrials.gov?
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
It’s the law (a final detail)

Some Phase I trials, though they are not Applicable Clinical Trials under FDAAA, are required to register under FDAMA – the earlier law -- which is still in effect.

These involve primarily experimental treatments for serious or life-threatening diseases whether using an IND, Group C Cancer drug, or other FDA regulated product.

Thus, many studies for cancer and other serious and life-threatening diseases must register regardless of Phase.

For more information:

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 6 months (30 days for Recruitment Status and Primary Completion Date)

http://grants.nih.gov/clinicaltrials_fdaaa/ACTs_under_FDAAA.htm
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
  o Pending publication is NOT considered a good cause for delay

http://clinicaltrials.gov/ct2/manage-recs/fdaaa
#2 You Want to Publish!

**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](http://www.icmje.org/journals.html)
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
ICMJE - Registration

- When to register:
  - Prior to enrollment of 1st subject
- ICJME 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
Policy Requirements – Recap  
(Relative numbers of trials subject to policy)

- FDAAA Results & AE Reporting
- FDAAA and FDAMA Registration
- ICMJE Registration
Who is responsible for registering?
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 (here at OSU the principal investigator)

http://grants.nih.gov/clinicaltrials_fdaaa/Responsible_Party.htm
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 “Ohio State University”
  - Ohio State University Medical Center PI is the responsible Party
Who is the RP? (Let’s practice)

1. Department funded/ PI initiated research
2. NIH funded research/ Ohio State University Medical Center is the grantee institution the Principal Investigator resides at OSU
3. Pharmaceutical company funded research/ multi-center study including site at Ohio State University
4. Device company funded research/ Ohio State University PI is the IDE holder
5. Cooperative Group study
What happens if I don’t register?
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
What are my responsibilities for the following studies? Hmmm…
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?
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?
Study #3

Assess the impact on Quality of Life (QoL) of long term caregivers of patients with multiple sclerosis.

• Centers/sample size: Multi-site, 450 subjects
• Intervention/method: Caregivers take QoL survey monthly for 2 years
• Other fact: Funded by Pharmaceutical Co.

Register? For FDAAA? For ICMJE? Results? Responsible Party?
Study #4

Implantable device designed to relieve the symptoms of heart failure through counter-pulsation technology.

- Study Design: Open Label
- Intervention: Implantable device (IDE obtained)
- Primary outcome: to test the feasibility of the device
- 8 people enrolled, 6 month study

Register? For FDAAA? For ICMJE? Results? Responsible Party?
Study #5

Dental graduate student is the investigator for a medical device study.
• Study Design: Randomized
• Intervention: Treatment with 1 of 3 different FDA approved medical devices
• Primary Outcome: Which device increases fluoride in saliva the most?

Register? For FDAAA? For ICMJE? Results? Responsible Party? Who will follow up when she graduates?
Hip Fracture Study

- Method: Compile data from electronic medical record (EMR) over a two year period for 1700 subjects
- Data elements: smoking status, use of alcohol, bone marrow density, weight, and height
- Primary Outcome: Determine the validity of a new hip fracture risk assessment method compared to FRAX, World Health Organization’s fracture risk tool

Register? For FDAAA? For ICMJE? Results? Responsible Party?
What is the FDAAA requirement for informed consent language?
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](http://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 Ohio State University IRB office or office of regulatory affairs.
“As required by law”

- Note: you should only include that section if the trial is an “applicable clinical trial” required by law to post in ClinicalTrials.gov.

- If not, do not use this language.

Guidance for Sponsors, Investigators, and Institutional Review Boards
Questions and Answers on Informed Consent Elements, 21 CFR § 50.25(c)
(Small Entity Compliance Guide) Feb. 2012
Nonbinding on government!
Reasons to Register & Use Informed Consent Language

FDAAA Results & AE Reporting

FDAAA and FDAMA Registration

ICMJE Registration

Looking for Participants
What if I have more questions?
Additional Resources

- Ohio State University College of Medicine, Office of research
  [http://medicine.osu.edu/research/clinical_research/clinical_trials/pages/index.aspx](http://medicine.osu.edu/research/clinical_research/clinical_trials/pages/index.aspx)

- General ClinicalTrials.gov information: [http://clinicaltrials.gov/ct2/about-site](http://clinicaltrials.gov/ct2/about-site)


- For specific questions or comments: [register@clinicaltrials.gov](mailto:register@clinicaltrials.gov).


Ohio State University Administrators

For Additional Questions
please contact:

For College of Medicine Principal Investigators please contact Meliha Rahmani 292-4876

For Comprehensive Cancer Center Principal Investigators please contact Lisa Brenner 293-7843

For Principal Investigators from all other colleges please contact Sandra Meadows 688-8641
Steps to Obtaining an Account @ OSUWMC

Step 1: Determine if you are responsible for registering your clinical trial on clinicaltrials.gov

only register trial's if OSUMC is the responsible party definition: (https://register.clinicaltrials.gov/prs/html/definitions.html#RespParty)

STEP2: Contact A Clinicaltrials.gov Administrator
Vanessa M. Hill : Vanessa.hill3@osumc.edu
Or
Mehdi Rahmani : Mehdi.rahani@osumc.edu

Information Needed
1. Full Name, University Title, Department & contact Info
2. Project Title, IRB Number

Step 3: Once an account is created you will receive an email with username and password to log into the PRS System: https://register.clinicaltrials.gov/
Log in and change your password, keep your password as you will need this to maintain the trial records

Step 4: For modifying an existing protocol go to section titled Protocol Records click on Modify and follow instructions

Step 4: For creating a new protocol record go to section titled Protocol Records click on create and follow instruction (only 1 record is needed in clinicaltrial.gov for a protocol)
Proceed as directed

Standard Functions

Protocol Records
Create
Modify
View
QA Review Comments
Required Personal ClinicalTrials.gov PRS

- **Study Owner:** Can either be the PI or a designated individual. The study owner has access to update the study record and regulate who has access to the record. (If one needs to change study owner contact your administrator)

- **Responsible Party:** If it is an Investigator Initiated study then the Principal Investigator is the Responsible Party. The responsible party has the sole authority to release a record.
Common Questions for your Administrator
I don’t see any problems with my record why are you contacting me?
Most likely it is time for a regular update

- Once you are logged into your account any records with issues per the PRS System will be listed, the general topic where the issue exists will also be listed.

Protocol Records
- Create
- Modify
- View
- QA Review Comments
- Problems: RahmaniM Records
- Undelete

- Pending QA Review Comments
- Not Completed
- Late Results - per FDAAA
- Update Not Released
I have no updates, what is required by PRS?
If nothing has changed and no other updates are required update the Record Verification Date to current month and year and have PI confirm and release.

| **Edit** | 
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Record Verification Date:** | January 2013 |
| **Overall Status:** | Completed |
| **Study Start Date:** | February 2007 |
| **Primary Completion Date:** | June 2010 [Actual] |
| **Study Completion Date:** | June 2010 [Actual] |
I do not understand where I can find the QA comments PRS wants addressed?
Quality Assurance Review:  QA Review Comments  History

View Comments Recorded:
Mar-05-2013 15:47:38.0
Jan-23-2013 14:45:58.0
Dec-04-2012 12:06:58.0
Dec-14-2011 09:21:11.0
Sep-16-2011 14:12:04.0
I have created a new study record and my PI is unable to see the record?
Most likely you forgot to add them to the access list, even though they are the responsible party, access is not granted until the study owner adds them to the access list.

[Access List] Last updated: 02/27/2013 10:00
I forgot my log-in details?
Please contact your Administrator, we can provide you these details and help to reset your password
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