Why Does it Affect Me?
Should I Be Concerned?
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 YOUR INSTITUTION
- Help Resources (institutional & national)
What is ClinicalTrials.gov?

Why should I be concerned?
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
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  
Ottawa Statement  
World Health Organization (WHO)

ClinicalTrials.gov

Recruitment (e.g., patients, physicians)  
Journal Editors  
Researchers & Funders  
Institutional Review Boards (IRBs)  
Health Policymakers

Why should I register a trial in ClinicalTrials.gov?
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 12 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
  - Pending publication is NOT considered a good cause for delay

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

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 PI is the Responsible Party
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
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 “YOUR U” 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)
*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

- General ClinicalTrials.gov information: http://clinicaltrials.gov/ct2/about-site
- FDAAA related information: http://clinicaltrials.gov/ct2/manage-recs/fdaaa
- For specific questions or comments: register@clinicaltrials.gov.
- Office of Extramural Research (OER): http://grants.nih.gov/Clinicaltrials_fdaaa/
- Instructions for Authors sections of ICMJE journals all have information regarding clinical trial registration
OSUWMC Administrator

For Additional Questions please contact:
Meliha Rahmani MPH, CCRC

Meliha.Rahmani @osumc.edu

or

Call: 614-292-4876
Steps to Obtaining an Account @ OSUWMC

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

Step 2: Contact a Clinicaltrials.gov Administrator
- Vanessa M. Hill: Vanessa.hill3@osumc.edu
- Meliha Rahmani: Meliha.rahmani@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.

Standard Functions:
- Create
- Modify
- View
- QA Review Comments

For creating a new protocol record, go to section titled Protocol Records, click on create and follow instructions (only 1 record is needed in clinicaltrials.gov for a protocol)
Proceed as directed.
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