

Clinical Trial Disclosure Investigator Training

January 2012



YOUR MISSION | OUR SOLUTIONS

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Philosophy of Knowledge

“Knowledge is of two kinds. We know a subject ourselves, or we know where we can find information upon it.”

- Samuel Johnson (1709-1784)
British author, lexicographer

Agenda

- Background on Clinical Trial Registration/Reporting regulations
- FDAMA and FDAAA Requirements
- ICMJE and Clinical Trial Registration
- Results Reporting
- Grant Requirements
- Informed Consent
- Yale University Status of Registration and Reporting
- Consequences of Noncompliance

Objectives

- Provide an understanding of current regulations related to Clinical Trial Registration and Reporting
- Understand the implications of non-compliance
- Motivate research teams to maintain a close eye on registration and results reporting for their trials
- Provide advice regarding how to make the registration and results reporting process go smoother

My Background

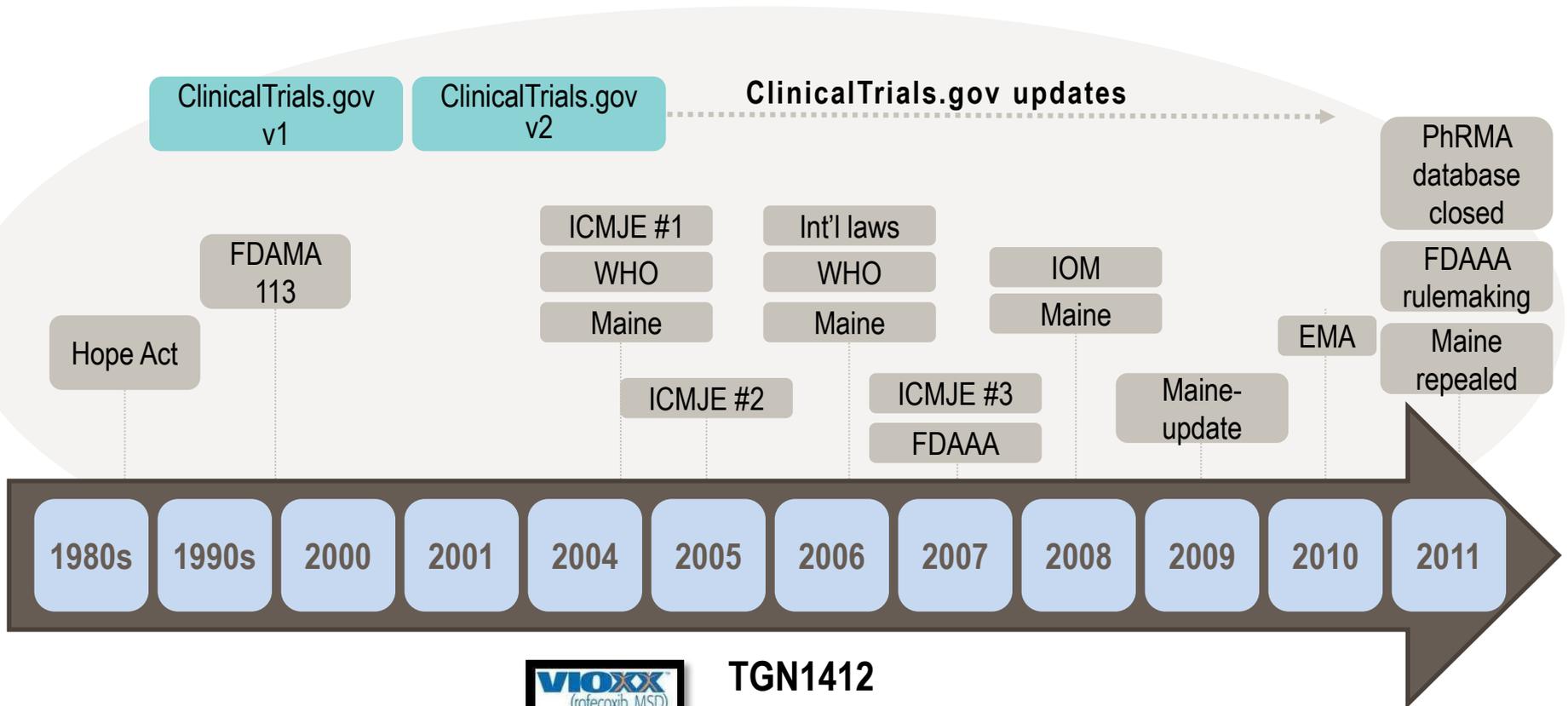
Background

- 12 years of clinical/surgical experience
- Additional 17 years specializing in domestic and international clinical trial disclosure policies, processes, and regulations, and medical writing
- Current Chair of the Drug Information Association's Clinical Trial Disclosure Special Interest Area Community
- Pharmaceutical industry: led the development of the operations group for clinical trial disclosure at Novartis Pharmaceuticals Corporation
- Peer-reviewed publications

Education and certification

- BA, Colorado State University
- Diploma in Nursing, Mennonite Hospital School of Nursing
- Medical Writing Certificate, Graham School, University of Chicago,

Clinical Trial Disclosure History



How Did We Get Here?

- International Committee of Medical Journal Editors (ICMJE): Inconsistent reporting of protocols and results to top-tiered journals
- New York State Attorney General (and others): High-profile legal action against large pharmaceutical companies
- Office of Inspector General: Corporate integrity agreements
- FDA Compliance Program Guidance Manual with disclosure language
- Loss of public trust/confidence in clinical research industry since 1998¹
- Loss of public trust/confidence in FDA²
- Demand for more transparency in drug development and clinical research process

¹Getz K. Public confidence and trust today: a review of public opinion polls. 2008. www.ciscrp.org

²Harris Interactive. Lack of trust in the FDA and pharmaceutical companies makes drug safety a concern for many. Healthcare News. 2007; 7(6)1-5.

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FDAMA Section 113

Food and Drug Administration Modernization Act (1997)

- Investigational New Drug (IND) application involving a drug
- Trial treats a serious or life-threatening disease or condition
 - FDA defines “life-threatening” as (1) diseases or conditions where likelihood of death is high unless course of disease is interrupted and (2) diseases/conditions with potentially fatal outcomes, where endpoint of clinical trial analysis is survival.
 - FDA considers “seriousness” of a disease a matter of judgment, but is generally based on survival, day-to-day functioning, and likelihood that, if left untreated, disease will progress to a more serious condition (e.g., AIDS, HIV, Alzheimer's disease, heart failure, cancer, etc.). FDA also notes that chronic, but well managed, illnesses can have serious outcomes (e.g., inflammatory bowel disease, asthma, rheumatoid arthritis, diabetes mellitus, depression, psychoses, etc.).
- Trial tests effectiveness
- FDA considers all Phase II, Phase III, and Phase IV trials with efficacy endpoints as trials to test effectiveness.
- Phase I trials with efficacy endpoints may qualify (e.g., oncology, AIDS, etc.)

FDAAA Section 801: Registration of Applicable Clinical Trials*

Food and Drug Administration Amendments Act (2007)

WARNING: Complex definition simplified!

■ Registration

- Phase II, III, and IV interventional trials in drugs, biologics, or devices subject to FDA regulation
 - Conducted under an IND or investigational device exemption (IDE)
 - With one or more sites in the US
 - Compound manufactured in the US (or its territories)
 - Conducted outside US, but within FDA jurisdiction
 - Clinical investigation of a drug can be an applicable clinical trial (ACT) under FDAAA even if it does not require an IND (e.g., **Phase IV investigator-initiated trial not looking at new use/indication**)
 - Trials must be registered within 21 days of study start
- Trials that **DO NOT** require registration according to FDAAA
- Phase I trials (may need to register to meet FDAMA)
 - Observational studies

*Draft Elaboration of Definitions of Responsible Party and Applicable Clinical Trial. March 29, 2009.

<http://prsinfo.clinicaltrials.gov/fdaaa.html>. Subject to change based upon rulemaking

FDAAA Section 801: Results Reporting of Applicable Clinical Trials*

Food and Drug Administration Amendments Act (2007)

WARNING: Complex definition simplified!

■ Results reporting

- Same conditions for registration, but results are reported for Phase II, III, and IV interventional trials in **marketed** products or for a **new use/indication** in drugs, biologics, or devices
- Most results submissions to ClinicalTrials.gov due no later than 12 months after primary completion date
 - **Primary completion date:** *Last visit of last patient specifically for purposes of data collection for primary outcome measure of the trial--NOT to be confused with “Last Patient Last Visit”*
- Delayed disclosure possible for products not yet approved
- Results for unapproved products generally due 30 days after receipt of complete response letter from FDA

*Draft Elaboration of Definitions of Responsible Party and Applicable Clinical Trial. March 29, 2009.

<http://prsinfo.clinicaltrials.gov/fdaaa.html>. Subject to change based upon rulemaking

Is it an Applicable Clinical Trial?

Does the trial include a drug, biologic or device?

Yes

No



Not considered an ACT

Drug/Biologic

Does trial meet all of these four criteria:

1. It is a clinical investigation
2. It is a controlled clinical investigation
3. It is other than a Phase 1 clinical investigation
4. It investigates a drug (including a biological product) subject to section 505 of the Federal Food, Drug, and Cosmetic Act (FDC Act) or section 351 of the Public Health Service Act

Yes

No



Would be considered an ACT



Not considered an ACT

Device

Does device trial meet all of these four criteria:

1. It is a prospective clinical study of health outcomes
2. It compares an intervention with a device against a control in human subjects
3. The studied device is subject to section 501(k), 515, or 520 (ms) of the FDC act
4. It is other than a small clinical trial to determine the feasibility of a device or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes

No

Yes

Is it pediatric post market surveillance as required under section 522 of the FDC Act?

Yes

No



Not considered an ACT



Would be considered an ACT

This flow chart may not address every situation. The grantee's sponsored research office, general counsel, or other similar official should be involved in determining whether or not the grant supports an applicable clinical trial that needs to be registered under FDAAA.

http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf

Applicable Clinical Trials and Responsible Parties

Additional information and resources

- For more detailed information

<http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf>

DRAFT	March 9, 2009
ELABORATION OF DEFINITIONS OF RESPONSIBLE PARTY AND APPLICABLE CLINICAL TRIAL	
<p>The elaboration of definitions of “Responsible Party” and “Applicable Clinical Trial” represent the National Institutes of Health's (NIH's) current thinking on this topic. They do not create or confer any rights for or on any person and do not operate to bind NIH, the Department of Health and Human Services or the public. NIH will interpret these terms in regulations or guidance to be issued at a later date. Prior to the issuance of draft regulations or guidance for comment, comments on these draft definitions are welcome and should be addressed to register@clinicaltrials.gov. Please include “Comment on Elaborated Definitions” in the subject line.</p>	

Still in draft form, but active guidance

- For a tool to assist identifying ACTs

http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm

*Draft Elaboration of Definitions of Responsible Party and Applicable Clinical Trial. March 29, 2009. <http://prsinfo.clinicaltrials.gov/fdaaa.html>. Subject to change based upon rulemaking

Responsible Party

Are you the responsible party?

■ The Sponsor

- Defined by ClinicalTrials.gov as **the company/organization/agency that initiates the trial (not the party who provides funding for the trial)**
 - Multicenter trials: generally pharma/biotech/medical device company/organization
 - Can also be an individual who initiates a trial, but has someone else conduct the investigation (i.e., pharma company that employs a CRO to conduct the trial)
 - NIH/FDA considers holders of an Investigational New Drug (IND) or Investigational Device Exemption (IDE) the sponsor (i.e., sponsor-investigator)

■ The Principal Investigator

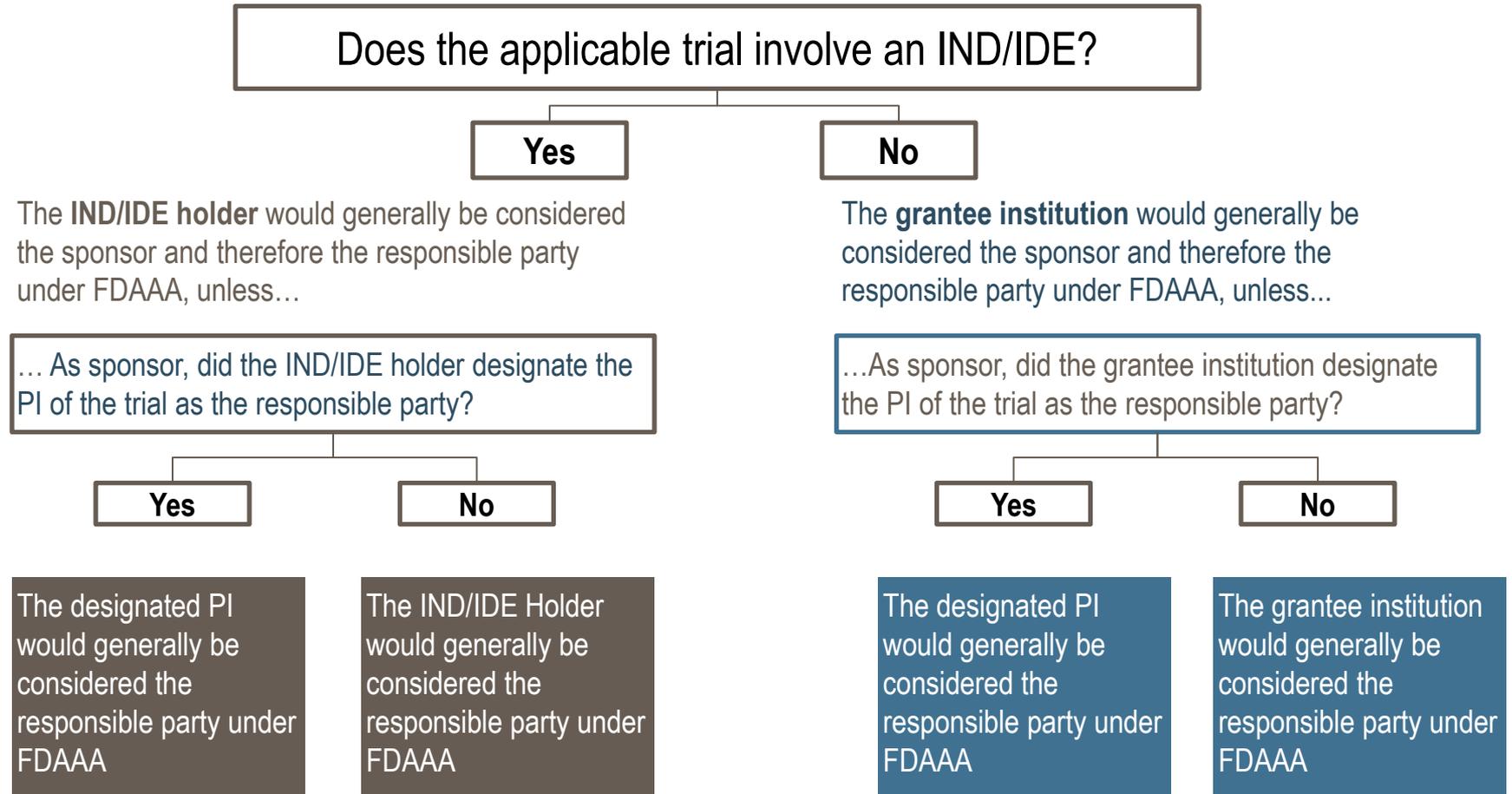
- If the principal investigator is responsible for **conducting the trial, has control over the data** from the trial and has the **right to publish the results** of the trial
- The principal investigator will need to release the record to ClinicalTrials.gov. The administrator can update the record, mark the record as completed and can approve the record, but **only the principal investigator (i.e., Responsible Party) can release the record**

On Being the Responsible Party

- For extramural trials, where there is no IND or IDE holder, NIH is not the “responsible party.” Funding recipient may be a responsible party depending on the unique circumstances of the trial.
- Responsible party must certify in grant application/progress reports that all required submissions have been made to ClinicalTrials.gov for ACTs funded in whole/part by any agency of the Department of Health and Human Services (FDA Form 3674).
- Consult with sponsored research office, institutional counsel, or other partners to determine if you are the responsible party.
- Tool to assist in identifying responsible party:
http://grants.nih.gov/ClinicalTrials_fdaaa/Responsible_Party.htm

Responsible Party

Identifying the responsible party



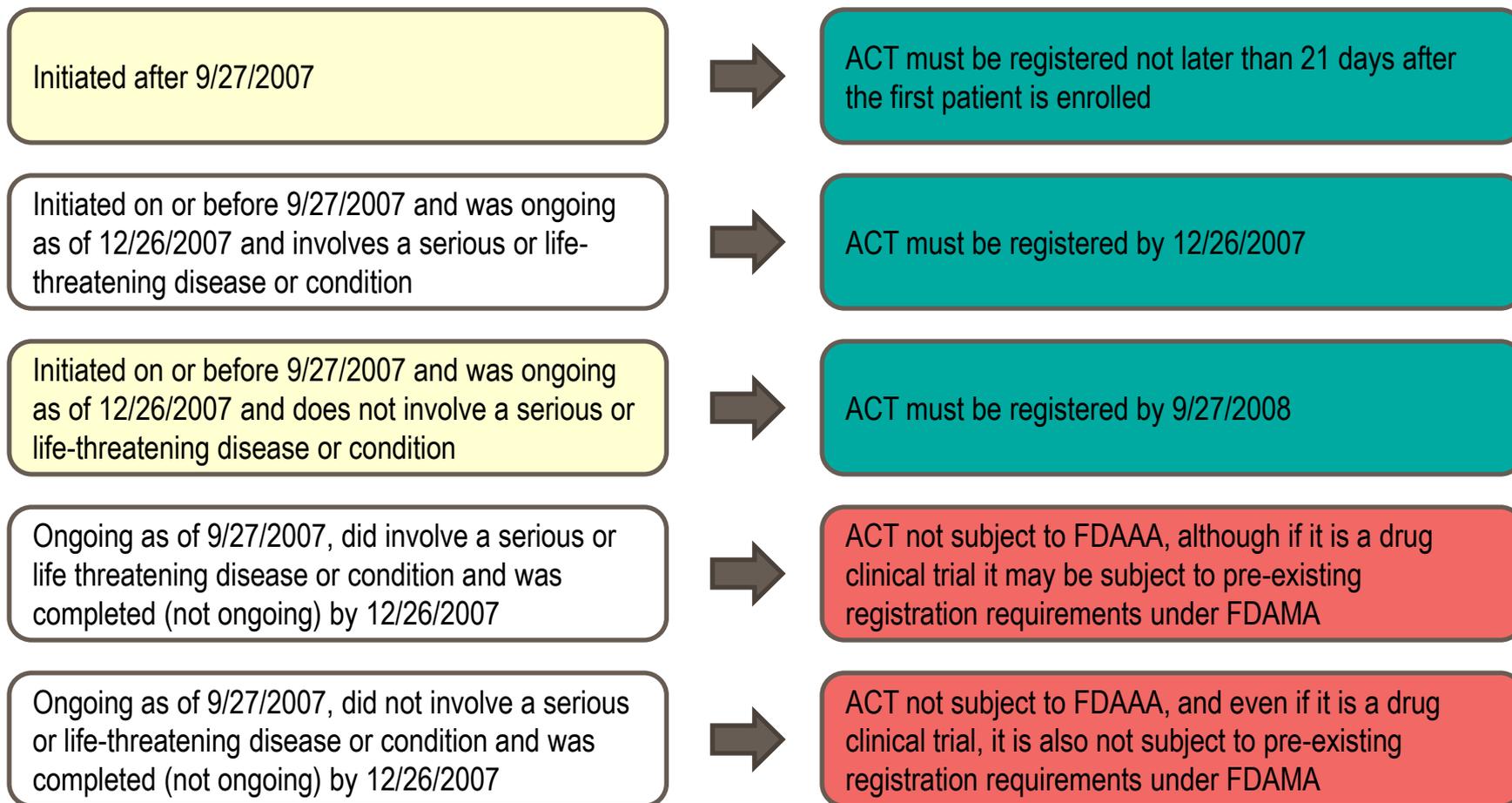
This flow chart may not address every situation. The grantee's sponsored research office, general counsel, or other similar official should be involved in determining whether or not the grant supports an applicable clinical trial that needs to be registered under FDAAA.

http://grants.nih.gov/ClinicalTrials_fdaaa/docs/registration_flow_chart.pdf

FDAAA Timelines

Criteria to determine if (and when) the ACT needs to be registered under FDAAA

If trial was...



This flow chart may not address every situation. The grantee's sponsored research office, general counsel, or other similar official should be involved in determining whether or not the grant supports an applicable clinical trial that needs to be registered under FDAAA.

http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf

Importance of Registering Trials

Patients, publications, and principles

- ICMJE
 - Allows for verification of trial's objectives against what manuscript reports
 - Early registration mandate window allowed some flexibility in accepting manuscripts with retrospective registration
 - Early flexibility now replaced with relative rigidity; some anecdotal inconsistency noted
- FDAMA and FDAAA require registration
- Patients: Informs patients and healthcare professionals of ongoing clinical trials

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ICMJE Stance on Protocol Registration

- ICMJE believes that it is important to foster a comprehensive, publicly available database of clinical trials.
- **Trials must be registered before study start.**
- Defines a clinical trial as *any* research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome.
- Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, etc.
- Registry must be free, publically accessible, managed by a not-for-profit organization, and open to all prospective registrants.
- Advocates use of ClinicalTrials.gov to comply with FDAAA.

Goes beyond FDAAA

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

- Obligation to register clinical trials:
http://www.icmje.org/publishing_10register.html
- Questions about clinical trial registration:
http://www.icmje.org/faq_clinical.html
- DeAngelis C, Drazen J, Frizelle F, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *New Engl J Med*. 2004;351:1250-1251.
- DeAngelis C, Drazen J, Frizelle F, et al. Is this clinical trial fully registered? — A statement from the international committee of medical journal editors. *N Engl J Med* 2005;352;2436-2438.

Will ICMJE Publish Results Posted to ClinicalTrials.gov?

Definitely!

- ICMJE understands problems associated with posting research results without an independent peer-review process and acknowledges FDAAA mandate of posting summary results data to ClinicalTrials.gov.
- **ICMJE does not consider results data posted in the tabular format required by ClinicalTrials.gov to be prior publication.**
- If you have an important and robust trial of a drug or device that you would like published before disclosing the results on ClinicalTrials.gov, contact the journal early and request fast track review.
- BMJ openly states they do not turn down trials that have already been disclosed on ClinicalTrials.gov.
- **Will these policies change if technical summary is added via rulemaking?**

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2011 Data on Results Reporting for ACTs

As of September 7, 2011

Data Provider	FDAAA Registration Analysis		FDAAA Results Analysis		All Studies Total Results Submitted ³
	Registered ACTs ¹	Primary Completion Date Listed	ACTs Appearing to Need Results, Certifications, or Extensions ²	ACTs with Posted Results, Certifications, or Extensions	
Industry	10,660	8,916 (84%)	4,395	2,245 (51%)	4,028
Non-Industry	14,369	11,791 (82%)	4,298	544 (13%)	1,815
Total	25,029	20,707 (83%)	8,693	2789 (32%)	5,843

¹ Approximate ACTs - registered interventional studies of drugs, biologics, devices that are “not Phase 0 or 1”, not “Withdrawn”, have at least one US location or IND/IDE with either a Primary Completion Date \geq 1/2008 or Study Completion Date \geq 1/2008 or both completion dates missing.

² Based on estimated registered approximate ACTs with a Primary Completion Date prior to August 2010.

³ Submitted includes all “posted” and “not yet posted” records that may or may not be subject to FDAAA. Results are reviewed by NLM prior to posting and most records require one or more revisions.

Williams, R. Asst. Director, ClinicalTrials.gov. The Evolving Clinical Trial Disclosure Landscape. Drug Information Association workshop. September 13-14, 2011. Arlington, VA.

Challenges in Results Reporting

- Importance of a well-written protocol with clear objectives/outcome measures cannot be understated
- Results for outcome measures with multiple time points: 1 outcome measure per time point
 - *EXAMPLE: [NCT00950599](#) has 84 secondary outcome measures*
 - **HINT:** Take care when developing protocols with multiple primary/secondary outcome measures.
 - Results from this trial took many weeks to enter the data.
- Simple protocol*: Gathering, entering, reviewing data for results record can take **20-30 hours** per trial depending on trial design
- Multiple review cycles with ClinicalTrials.gov QA staff likely
- Inflexible data fields and display in ClinicalTrials.gov

* 1 primary outcome measure, 2-3 secondary outcome measures

Challenges in Results Reporting

Academic Medical Centers

- Clinical trial reports not often written; not often used as a resource for data identification
- Data analyzed from data tables (SAS format, etc.)
 - Can make data identification challenging for results reporting for non-investigators
 - Can lead to transcription errors when entering into ClinicalTrials.gov
- **Principle investigators (or qualified designees) must be available to review draft results reporting with data entry staff and trial statistician**
- Differing definitions within institutions about “end of study”
 - “We’re still analyzing data so study isn’t done yet”– does not qualify
- Oncology trials: patients followed until death (which may be after primary completion date)

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Grant Applications Requirements

- For competing applications (new and renewal) that include ACTs:
 - NCT number
 - Brief title as defined by ClinicalTrials.gov
 - Identity of the responsible party (Human Subjects Section of the research plan)
 - If a new trial is proposed: Human Subjects Section of the research plan should include a statement that application includes a trial requiring registration in ClinicalTrials.gov.
- Requirements apply to all grant applications submitted to NIH on or after January 25, 2008 with an ACT in the proposed project
- If grant is for ACT, include a Certification of Compliance (FDA Form 3674) in competing grant application.

www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf

Progress Report Requirements

- Non-competing progress report that includes ACTs
 - NCT numbers
 - Brief Titles
 - Identity of the responsible party (Human Subjects Section of the research plan)
- Requirements apply to all progress reports for grants with ACTs with budget start dates of April 1, 2008 or later
- If grant is for ACT include a Certification of Compliance (FDA Form 3674) in progress report.

www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf

Certification of Compliance: Form 3674

Trial Types Expected on a 3674

- Investigational New Drug (IND) applications
- New clinical protocol submitted to an IND
- New Drug Application (NDA)
- Efficacy Supplement to an approved NDA
- Biologics License Applications (BLA)
- Efficacy Supplement to an approved BLA
- Abbreviated New Drug Application (ANDA)
- Premarket Approval (PMA)
- PMA Panel Track Supplement
- Humanitarian Device Exemption (HDE)

www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf

Helpful Hints about Grants (1)

- Determine if competing application/funded grant supports an ACT.
- Include a Certification of Compliance (FDA Form 3674) in competing grant application and progress report.
- If grant supports an ACT, determine the responsible party.
- If the grantee is not the sponsor and not the responsible party, contact the responsible party to ensure that the trial is registered and results are reported.
- Responsible party must register the ACT no later than 21 days after enrolling the first subject (**ICMJE requirements differ!**).
- Responsible party must regularly update information in the ACT record.
- Responsible party must report ACT results not later than 1 year after the primary completion date.

Helpful Hints about Grants (2)

- If more than one award supports a non-IND/IDE ACT, investigators and institutional officials associated with the trial must work together to determine the responsible party, and to coordinate and communicate the determination with other grantees
- NIH cannot register/report results for ACTs when the NIH is not the responsible party
 - Previous NIH-established mechanisms to directly assist funding recipients in registering and reporting results are no longer supported
- Costs of FDAAA compliance will be generally be allowable as direct charges to NIH supported grants. While it is expected that these costs will be covered by the funds provided with the grant, **administrative supplements could also be considered.**

http://grants.nih.gov/ClinicalTrials_fdaaa/faq.htm

Helpful Hints about Grants (3)

- If you are the PI on an NIH grant, but not the responsible party for the ACT the grant supports and the trial is not in compliance with FDAAA, **you cannot register the trial**. You should work with your organization to identify the responsible party to encourage compliance.
- All grant-funded ACTs must report results information (including adverse events) no later than 1 year after the primary completion date. However, NIH encourages results reporting for all NIH-supported clinical trials registered in ClinicalTrials.gov, regardless of whether or not they are required to do so under FDAAA.

Helpful Hints about Grants (4)

- Responsible party may submit a certification for delayed submission of results information for an ACT that is:
 - completed before the drug or device is initially FDA-approved, licensed, or cleared ("seeking initial approval")
 - studying a new use of an FDA-approved drug or device ("new indication")
 - Director of NIH may provide an extension for results reporting if the responsible party submits a written request that demonstrates good cause (e.g., natural disaster and data is lost [hurricanes, etc.]) and provides an estimate of the date on which the results information will be submitted. **Pending publication is not considered a good cause for an extension.**

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Informed Consent

- **Exact** language from the FDA's Compliance Program Guidance Manual (11 March 2011) to be included on informed consents for ACTs:
“A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”
- If you amend informed consents for non ACTs, you are obligated to post the information to ClinicalTrials.gov.

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Yale's Current Status on ClinicalTrials.gov

Registered, reported, and unknown as of January 3, 2011

- 353 protocols registered on ClinicalTrials.gov
 - 307 interventional trials—**active registration is great!**
 - # of ACTs ??? (analysis pending)
- 4 results postings
 - # of ACTs delinquent in results posting??? (analysis pending)
- ~87 Yale registered protocols with “unknown” status
 - Public view on ClinicalTrials.gov website will show “status = unknown” for records that have not been updated or verified in >2 years
 - What does “unknown” convey to public about Yale’s diligence?—not so good...
- >10,000 non-industry records with unknown status
- ~2,300 industry records with unknown status

Tips on Finding Help at Yale

- Yale has ~265 registered users of ClinicalTrials.gov familiar with aspects of entering data/registering protocols into the system
- ClinicalTrials.gov has >4800 trials with results posted
 - Consider looking at some of those results reports to find one similar to your trial design and use it as an example for results reporting
 - Helps to identify the type of data in the format ClinicalTrials.gov requires
 - ClinicalTrials.gov has guidance forms in their protocol registration system.
- Additional training and guidance forms available through Yale Center for Clinical Investigation
 - Tesheia Johnson
 - Kevin Palmer
- Additional questions about ClinicalTrials.gov requirements: NIH Office of Extramural Research at OEPmailbox@mail.nih.gov.

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Legal Consequences of Not Noncompliance

Grant recovery and legal fines

- FDAAA fine for not registering or reporting trials: potential for **\$10,000/day fine**¹
- **Withholding remaining or future grant funding or recovery of monies already allocated**²
- NIH will verify that each ACT for which the grantee is the responsible party has been registered in ClinicalTrials.gov

¹Food and Drug Administration Amendments Act of 2007. Public Law No. 110-85, Section 801.

²<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-023.html>

ICMJE Consequences of Not Registering Trials

Are they serious about not publishing unregistered trials ?

- Not registering the trial on ClinicalTrials.gov prior to study start almost certainly disqualifies your manuscript from publication.
- **BMJ has rejected 10-20 manuscripts/year for failing to register a clinical trial prospectively** in line with ICMJE policy.¹
- **To date (Nov 2011), NEJM has rejected 66 papers for registration issues** (8 for lack of proper registration, 58 for late registration) and have not granted appeals.²
- **Yale has had manuscripts rejected from NEJM for noncompliant protocol registration**

¹Personal communication between Barbara Godlew and Pamela Miller, NEJM. 28 Nov 2011.

²Personal communication between Barbara Godlew and Trish Groves, BMJ. 28 Nov 2011.

Public Relations Consequences of Noncompliance

Can Yale afford negative press?

By Michael R. Law, Yuko Kawasumi, and Steven G. Morgan

DOI: 10.1377/hlthaff.2011.0172
HEALTH AFFAIRS 30,
NO. 12 (2011): 2338–2345
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The People-to-People Health
Foundation, Inc.

Despite Law, Fewer Than One In Eight Completed Studies Of Drugs And Biologics Are Reported On Time On ClinicalTrials.gov

EP Clinical TrialsSM
Powered by EvaluatePharma®

NEW SURVEILLANCE TOOL

Tired of mining clinical trial data from public sites? We do the work so you don't have to.

- Updated daily with unrivalled access to cross-linked trial records of ClinicalTrials.gov¹ and EudraCT²
- Clinical Trials.gov coverage includes 115,000+ trials, 20,000+ linked sources, 175+ countries, 90,000+ trial investigators, 640+ indications, mapped to 3200+ commercial companies

The current low rate of results reporting on ClinicalTrials.gov, particularly for studies not funded by industry, is troublesome and may affect the overall usefulness of the registry in expanding clinical knowledge in a timely manner.

High Profile Issue Problem: BMJ January 2012

Perception of selective reporting remains

- Compliance with mandatory reporting of clinical trial results on ClinicalTrials.gov: cross sectional study. BMJ 2012;344:d7373. <http://www.bmj.com/content/344/bmj.d7373>
 - Studies registered on ClinicalTrials.gov with US sites completed between 1 January and 31 December 2009.

Funder	# with results	Total	Percentage
Industry	126	317	40
Mixed	25	265	9
NIH/government	4	48	8
Other	8	108	7
Total	163	738	22

- Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012;344:d7292. http://www.bmj.com/highwire/filestream/554658/field_highwire_article_pdf/0.pdf
 - <50% of NIH-funded trials registered in ClinicalTrials.gov after Sept. 2005 and completed by Dec. 2008 were published in a peer-reviewed journal within 30 months of trial completion
 - ~30% of NIH-funded trials remained unpublished 51 months after trial completion

Final Considerations

Progress being made—more work to be done

- Is it worth the risk?
 - Trial findings not published due to lack of or late registration
 - Clinical trial funding wasted because publication denied
 - Loss of or repayment of federal grants for noncompliance
- Have you (or someone you know) been denied publication consideration by top-tier journal for not adequately registering your trial?

Red Flags to FDA

- Reports from NIH on sponsor activity/inactivity
- Form 3674 completed inaccurately
- Inconsistent reporting of protocols, results, journal articles on and between public databases (ClinicalTrials.gov, EU CTR, country-specific)
- Submission of minimal/vague data for review to public databases
- Not updating postings on regular basis (eg, “unknowns”)
- Lack of a clear institutional process/policy
- Investigations of other areas in the institution
- Inconsistency with informed consent language
- Whistleblowers

Additional References (1)

- Food and Drug Administration Amendments Act of 2007. Public Law No. 110-85, Section 801.
- Food and Drug Modernization Act (FDAMA) of 1997. Section 113. Public Law No. 105-115.
- Guidance for Industry: Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions. U.S. Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research (CDER). Center for Biologics Evaluation and Research (CBER). March 2002.
- ICMJE Questions about Clinical Trials Registration:
http://www.icmje.org/faq_clinical.html

Additional References (2)

- Presentations with audio and slides relevant to providing data to ClinicalTrials.gov:
 - [Overview of ClinicalTrials.gov](#)
 - [Key FDAAA Issues](#)
 - [Protocol Registration System Information and Data Review Process](#)
 - [Protocol Registration System Accounts and Registration](#)
 - [Results: Participant Flow Module](#)
 - [Results: Baseline Characteristics Module](#)
 - [Results: Outcome Measures and Statistical Analyses Module](#)
 - [Results: Adverse Events Module](#)

Additional References (3)

- Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007
www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM164819.pdf
- Certification of Compliance with Requirements of ClinicalTrials.gov
www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048364.pdf

Additional References (4)

Informational forms

NOTE: You may receive a certificate error when clicking on these links. This is a safe ClinicalTrials.gov test database. If you receive a certificate error, select the following:  Continue to this website (not recommended).

Results section	Form	Link
Participant Flow	Part. Flow form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_PopFlowForm.pdf
Baseline	Required Age form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_BaselineAgeForm.pdf
	Required Gender form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_BaselineGenderForm.pdf
	Opt. Region/Race form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_BaselineRegionRaceEthnicityForm.pdf
	Opt. Study specific characteristics form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_BaselineSpecificCharForm.pdf
Outcome Measure	Outcome measure form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_OMForm.pdf
Adverse Events	SAE form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_SAEForm.pdf
	Other AE form	https://prstest.nlm.nih.gov/prs/html/DataEntryTable_FreqAEForm.pdf

Federal Government's Response to Original Mandate



“That’s our new mission statement.”

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THANK YOU!

HuronLifeSciences

Call for Additional Data: PLOS December 2011

Disclosing investigative site recruitment data?

- Dal-Re´ R, Moher D, Glud C, Treweek S, Demotes-Mainard J, et al. Disclosure of Investigators' Recruitment Performance in Multicenter Clinical Trials: A Further Step for Research Transparency. PLoS Med 8(12): e1001149. doi:10.1371/journal.pmed.1001149
- <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001149>
- ...sponsors should disclose recruitment targets of all site investigators on ClinicalTrials.gov before a trial starts as well as their final recruitment.
- Disclosing all site investigators' recruitment figures could prompt queries to the sponsor from the scientific community about regional subgroup analyses, to assess if ethnic or standard-of-care differences have an impact on treatment outcomes.