Navigating the Expanding Regulations of ClinicalTrials.gov Registration and Results Reporting

Anthony Keyes, MBA, PMP
Program Manager, Clinical Research Projects, Director, ClinicalTrials.gov Program, Institute for Clinical and Transitional Services (ICTR); Johns Hopkins University

April 24, 2018
About Advarra

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➢ Leverage mutual strengths in technology, regulatory expertise and customer service to serve increasingly complex research needs
About Advarra

- Combined 50+ years of experience
- Access to over 2,000 unique institutional research sites
- Global consulting services
- The industry’s most comprehensive and efficient technology
About Today’s Presenter

Anthony Keyes, MBA, PMP
Program Manager, Clinical Research Projects at Johns Hopkins University, Institute for Clinical and Translational Research

> Responsible for several ongoing School of Medicine-wide projects
> Has also served as a Study Coordinator and Research Manager
> Has 15 years’ experience in many aspects of clinical trial coordination and management
> Certified Project Management Professional and
> Has successfully completed several, large-scale projects.
> He founded and directs the Johns Hopkins ClinicalTrials.gov Program and co-chairs the National Clinical Trial Registration and Results Reporting Taskforce
> Received his MBA in Healthcare Management from the Johns Hopkins University, Carey Business School and a Bachelors of Biology from the University of Maryland, College Park.
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Institute for Clinical and Translational Services (ICTR)

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Clinical Research Compliance Specialists
ICTR
Disclosures

Co-Chair of the National Clinical Trials Registration and Results Reporting Taskforce

The views and opinions expressed in this presentation are mine alone and do not necessarily reflect the views and opinions of Advarra
Outline

- Overview and background
- Regulatory bodies
  - Rules to live by
  - Who’s watching?
- Challenges we all face
- Elements of a successful program
- Specifics (Why?, What?, Who?, When?, How?)
  - Tips and tricks to help you
First Things First

- There are 2 different systems
  - Public site: https://clinicaltrials.gov/
  - User site: Protocol Registration and Results System (PRS) https://register.clinicaltrials.gov/

- There are 2 basic functions of ClinicalTrials.gov
  - Registration (Creating and updating the record)
  - Results (To be done within 1 year of completion)
Protocol Registration and Results System (PRS)

Welcome to the ClinicalTrials.gov Protocol Registration and Results System (PRS).

Organization: JohnsHopkinsU
One-word organization name assigned by PRS (sent via email when account was created)
Username: AKeys
Password: ********
Forgot password

See Submit Studies on ClinicalTrials.gov for information on how to apply for an account, how to register your study, and how to submit results.
Send email to ClinicalTrials.gov PRS Administration

Contact ClinicalTrials.gov PRS
Org: JohnsHopkinsU User: AKeys Login
Email: akeys1@jhu.edu | Update |
Help us improve PPRS Survey

Quick Links
New Record
Admin Quick Reference
Problem Resolution Guide

Record List

https://register.clinicaltrials.gov/
## Overview and background

<table>
<thead>
<tr>
<th>Year</th>
<th>Entity</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>Congress</td>
<td>1st U.S. law to require trial registration (FDAMA)</td>
</tr>
<tr>
<td>2000</td>
<td>NIH</td>
<td>Releases ClinicalTrials.gov website</td>
</tr>
<tr>
<td>2005</td>
<td>ICMJE</td>
<td>Requires registration before enrollment</td>
</tr>
<tr>
<td>2006</td>
<td>WHO</td>
<td>All clinical trials should be registered</td>
</tr>
<tr>
<td>2007</td>
<td>CMS</td>
<td>PI must enroll qualifying clinical trials in ClinicalTrials.gov</td>
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<tr>
<td>2007</td>
<td>Congress</td>
<td>Expanded registration, submission of results and adverse events, civil penalties (FDAAA)</td>
</tr>
<tr>
<td>2008</td>
<td>NIH</td>
<td>Releases results database</td>
</tr>
<tr>
<td>2015</td>
<td>CMS</td>
<td>Mandatory Reporting of Clinical Trial Number on Claims</td>
</tr>
<tr>
<td>2017</td>
<td>FDA</td>
<td>Final Rule compliance date (April 18, 2017)</td>
</tr>
</tbody>
</table>

FDAMA: Food and Drug Administration Modernization Act  
NIH: National Institutes of Health  
ICMJE: International Committee of Medical Journal Editors  
WHO: World Health Organization  
CMS: Centers for Medicare & Medicaid Services  
FDAAA: Food and Drug Administration Amendments Act
Regulatory Bodies

• Per FDAAA, the Responsible Party for an Applicable Clinical Trial must submit required clinical trial information through the Protocol Registration and Reporting System (PRS) no later than 21 days after enrollment of the first participant.

• Per FDAAA, results reporting must be no later than one year after primary completion date

• Potential monetary penalty of $11,569 for noncompliance per day, per study

• As of January 2017 requires registration and results reporting for all clinical trials receiving funding

• Can withhold grant funding for investigators and institutions that are noncompliant
Trials that meet the clinical trial definition of The International Committee of Medical Journal Editors (ICMJE) that the investigator may wish to publish, must register the study on ClinicalTrials.gov prior to enrollment of the first participant.

Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS). The National Clinical Trial (NCT) number must be included on claims for items and services provided in clinical trials that are qualified for coverage.

Signatories to the May 18, 2017 WHO, International Clinical Trials Registry Platform (ICTRP) such as the Bill and Melinda Gates foundation requires registration and results reporting of our grantees.
Key Components of the FDA Final Rule


• Applies to Applicable Clinical Trials (ACTs)
• Registration must be within 21 days of first enrollment
• Record must be verified at least annually
• Record must be updated within 30 days (e.g., completion dates, recruitment status)
• Comments must be responded to within 15 calendar days (registration) or 25 calendar days (results)
• Results due 365 days from primary completion date
• Requires submission of full protocol and statistical analysis plan with submission of results information.
Complementary Policy

NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information
(NOT-OD-16-149) Released: September 21, 2016, Effective January 18, 2017

• Complementary to the Final Rule (released the same day)
• Applies to NIH-funded clinical trials regardless of study phase, type of intervention (even if not an ACT), includes behavioral interventions
• Does not apply to a clinical trial that uses NIH-supported infrastructure but does not receive NIH funds to support its conduct.
• Responsible Party is considered the Sponsor (“grantee organization for NIH-funded trials”)
• Requires reporting of baseline race and ethnicity data (if collected)
• “grantees are permitted to charge the salaries of administrative and clerical staff as a direct cost”
NIH Dissemination Plan

• Applicants seeking NIH funding will be required to submit a plan for the dissemination of NIH-funded clinical trial information that will address how the expectations of the policy will be met.

• Upon receipt of an award, an awardee will be obligated to adhere to their plan through the terms and conditions of the award.

• The required plan can be a brief statement explaining whether the applicant intends to register and submit results information to ClinicalTrials.gov as outlined in the policy.
Penalties Outlined in the Final Rule

• Under FDAAA an organization can be fined $11,569* per study/per day for any issue of noncompliance, not only late results

• NIH can withhold funding to organizations that are out of compliance
  – Francis Collins, NIH Director, published a viewpoint in JAMA with the following quote, “In addition, NIH will withhold clinical trial funding to grantee institutions if the agency is unable to verify adequate registration and results reporting from all trials funded at that institution.”

5/11/2018  https://www.federalregister.gov/documents/2017/02/03/2017-02300/annual-civil-monetary-penalties-inflation-adjustment
# Federal Requirements

<table>
<thead>
<tr>
<th>Entity</th>
<th>Registration</th>
<th>Results Reporting</th>
<th>Penalties</th>
</tr>
</thead>
</table>
| Food and Drug Administration (FDA)          | Within 21 days of enrollment      | Within 365 days of primary completion date for ACTs                               | • $11,569/study/day  
• Criminal proceedings                         |
| National Institutes of Health (NIH)         | Within 21 days of enrollment      | Within 365 days of primary completion date for clinical trials receiving NIH funding | Loss of grant funding (to include the institution) |
| National Cancer Institute (NCI)             |                                    | Within 365 days of primary completion date of NCI-supported clinical trials (in a peer-reviewed journal and/or ClinicalTrials.gov) | Loss of grant funding                                |
| Centers for Medicare & Medicaid Services (CMS) | All qualifying clinical trials    |                                                                                   | • Coverage denial  
• Costs and fraud investigations                |
# Other Stipulations

<table>
<thead>
<tr>
<th>Entity</th>
<th>Registration</th>
<th>Results Reporting</th>
<th>Penalties</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Health Organization (WHO)</td>
<td>Prior to enrollment</td>
<td>Within 365 days of primary completion date</td>
<td></td>
</tr>
<tr>
<td>International Committee of Medical Journal Editors (ICMJE)</td>
<td>Prior to enrollment</td>
<td></td>
<td>Ineligibility to publish</td>
</tr>
<tr>
<td>Foundations (i.e., Gates)</td>
<td>Study-specific</td>
<td></td>
<td>Loss of funds</td>
</tr>
</tbody>
</table>
ClinicalTrials.gov New Requirements

Two major changes impact applications submitted for due dates on or after January 25, 2018.

1. **Applicants are required to use FORMS-E.**

   New NIH "FORMS-E" Grant Application Forms and Instructions Coming for Due Dates On or After January 25, 2018 - NIH Guide Notice NOT-OD-17-062, Release Date: April 27, 2017

   **Focus of changes:**
   - Consolidation of human subjects, inclusion enrollment, and clinical trial information previously collected across multiple agency forms
   - Expansion and use of discrete form fields for clinical trial information to align with ClinicalTrials.gov (where possible) and position us for future data exchange with ClinicalTrials.gov
ClinicalTrials.gov New Requirements

2. Applications that include one or more clinical trials must be submitted in response to funding opportunity announcements (FOA) that allow for clinical trials.


Release Date: November 30, 2017

“NIH will require all applications involving one or more clinical trials be submitted through a Funding Opportunity Announcement (FOA) specifically designed and designated for clinical trials. This policy improves our ability to identify proposed clinical trials, ensure that key pieces of trial-specific information are submitted with each application, and uniformly apply trial-specific review criteria.”
ClinicalTrials.gov New Requirements

New ICMJE data sharing statement requirement for publications

- For trials that start enrolling participants on or after January 1, 2019, ICMJE will require data sharing statements in the ClinicalTrials.gov registration as a condition of publication
  - (These statements will be required in manuscripts submitted to ICMJE journals starting in July 2018)
- In ClinicalTrials.gov, the data sharing statement is entered in the IPD Sharing Statement module

Courtesy of Scott Patton (Stanford)
Watchful Eyes

Johns Hopkins University

163 of 193 (84%) trials reported late or not at all
49 (30%) results missing in 2015 and 2017
47 (29%) results missing in 2015; posted late as of 2017
8 (5%) results not required in 2015; missing in 2017
14 (9%) results not required in 2015; posted late as of 2017
45 (28%) results posted late before 2015
Open Letter to FDA Commissioner

TrialsTracker uses publically-accessible data and is updated daily

Encourage everyone to explore the website by searching for your institution

Considering sending PIs 3 months advance notice of pending results due

Send any discrepancies, concerns or questions to hello@ebmdatalab.net
Challenges

• High turnover among research staff
• Lack of communication and formal exit procedures for PIs and study team members leaving the institution
• Data stewardship (especially when PIs leave)
• Older records (require time and special attention)
• Lack of awareness of ethical and legal implications
• Competing academic, research, & clinical responsibilities among PIs
• Lack of training and/or statistical knowledge
• Lack of clarity or difficulty understanding different requirements
• Difficulty with the website
Meeting the Challenges

Each institution must decide

- What resources to dedicate
- Who will Champion (Senior Leader)
- Extent the Program will interface with other internal systems
- Institutional policies and SOPs
- Level of effort from PIs and study staff
- Enforcement
- 1,000,000 other small details
JHU ClinicalTrials.gov
Program Highlights

Program based in the School of Medicine, Institute for Clinical and Translational Research (ICTR)

- Centralized, Institutional funding
  - Economies of scale (learning curve)
  - Increase compliance and decrease liability
  - Institutional efficiencies and policies
  - Enforcement

- 2.0 Full-time Clinical Research Compliance Specialists:
  - Prince Nuamah, MD
  - Aliya Lalji, MD

registerclinicaltrials@jhmi.edu

https://ictr.johnshopkins.edu/programs_resources/programs-resources/regulatory-compliance-and-guidance/clinicaltrials-gov-program/
JHU Clinicaltrials.gov

Program Highlights

• For the PI/Study team, assistance with…
  – Registration
    • Account creation and maintenance
    • Initial registration
      – Required for Applicable Clinical Trials
      – Required for any clinical trial receiving full or partial NIH funding
    • PRS reviewer comments (now time-limited to 15 calendar days)
    • Update reminders (required every 12 months regardless of changes)
    • Changes to PI/Study team (including when a PI leaves)
JHU Clinicaltrials.gov
Program Highlights

- Results Reporting
  - Results reporting reminders (due 12 months after *primary completion date*) – Need to start 3-4 months early
  - Assistance with results reporting
  - Assistance with PRS reviewer comments (now time-limited to 25 calendar days)
  - Changes to PI/Study team (including when a PI leaves)
  - Direct services at $50 per hour (optional)

* Final data collection date for primary outcome measure.
Communication Process

1. The Program maintains a detailed database of all studies.

2. The Program will inform the PI, central contact, and record owner via e-mail #1 when a study needs attention.

3. If no response to the initial communication, a follow-up e-mail #2 will be sent with carbon copies to both Division/Department Director and Assistant Administrator.

4. At this point, if no action has been made, e-mail #3 will be sent with carbon copy to the Vice Dean of Clinical Investigation.
Internal Collaborations

IRB

• Updated Clinical Trials section of the application to create uniformity
• Program staff have “View only” access to all records in eIRB2 and archives
• Updated Johns Hopkins School of Medicine Policy 103.25 “Organization Policy on Registration of Clinical Trials” to be in accordance with the FDA Final Rule
• Pulled paper records from off-site storage to enable results reporting for older studies (JHM Policy is to retain records for at least 7 years)
• Created reports for
  • Changes in PI
  • Studies which have been terminated or expired
  • Studies which are identified as clinical trials, but have no NCT registration number
• Able to flag non-compliant studies – coming soon
Internal Collaborations

Clinical Research Management System (CRMS)

- Program staff have “View only” access to all records in CRMS
- Generated a list of all studies that have begun enrollment but do not have an NCT number in neither eIRB nor CRMS
  - Any internal system which tracks actual participant enrollment can be used to ensure FDA and ICMJE guidelines and regulations are followed
- Receiving weekly reports for these studies and assisting PIs with compliance in real-time
- Relying on annual continuing review to enforce registration is insufficient
Increasing Compliance – Decreasing Liability
Registration and Reporting Requirements

Registration and Reporting Requirements

Why Register and Report?

- Commitment to research participants
- Scientific validity/transparency
- Ethical standards
- Responsible stewardship of federal funds
- Help IRB assess value of new studies
- Required by law (FDAAA)
- Required for journal publication (ICMJE)
- Required by NCI
- Required for CMS
- Required by WHO
- Bill and Melinda Gates and several other foundations
What Trials to Register and Report?

1. Clinical Trials funded either in whole, or in part by National Institutes of Health (NIH) (applicable to all NIH-funded “clinical trials” independent of whether the study meets the definition of an applicable clinical trial)
What Trials to Register and Report?

Use the following four questions to determine the difference between a clinical study and a clinical trial:

1) Does the study involve human participants?
2) Are the participants prospectively assigned to an intervention?
3) Is the study designed to evaluate the effect of the intervention on the participants?
4) Is the effect being evaluated a health-related biomedical or behavioral outcome?

Note that if the answers to the 4 questions are yes, your study meets the NIH definition of a clinical trial, even if...

- You are studying healthy participants
- Your study does not have a comparison group (e.g., placebo or control)
- Your study is only designed to assess the pharmacokinetics, safety, and/or maximum tolerated dose of an investigational drug
- Your study is utilizing a behavioral intervention
What Trials to Register and Report?

2. Trials that meet the clinical trial definition of The International Committee of Medical Journal Editors (ICMJE) that the investigator may wish to publish:
   ICMJE journals will consider [for publication] trials beginning on or after July 1, 2005 only if registration occurred before the first patient was enrolled ("prospective registration").

http://www.icmje.org/about-icmje/faqsclinical-trials-registration/
What Trials to Register and Report?

3. Qualifying clinical trials which will render claims for items and services to the Center for Medicare and Medicaid Services (CMS):
   The National Clinical Trial (NCT) number must be included on claims for items and services provided in clinical trials that are qualified for coverage as specified in the "Medicare National Coverage Determination (NCD) Manual," Section 310.1

What Trials to Register and Report?

4. ‘Applicable Clinical Trials’ include the following:

- Trials of drugs/biologics. Controlled clinical investigations, other than phase 1 trials of drugs/biological products subject to FDA regs.
- Trials of devices. 1) Controlled trials with health outcomes of devices subject to FDA regulation (other than feasibility studies) and 2) pediatric post-market surveillance required by FDA
- The trial has one or more sites in the U.S.
- The trial is conducted under an FDA IND or IDE application
- The trial involves a drug, biologic, or device that is manufactured in the U.S. or its territories and is exported for research

ACT Wizard: [http://grants.nih.gov/clinicaltrials_fdaaa/docs/Flow_chart-ACT_only.pdf](http://grants.nih.gov/clinicaltrials_fdaaa/docs/Flow_chart-ACT_only.pdf)
Identifying an ACT under FDAAA [http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm](http://grants.nih.gov/ClinicalTrials_fdaaa/ACTs_under_FDAAA.htm)
What Trials to Register and Report?

5. Supported by a foundation who is a signatory to the May 18, 2017 WHO, International Clinical Trials Registry Platform (ICTRP).

Dr Trevor Mundel, President, Global Health, Bill & Melinda Gates Foundation
"It's a 21st-century best practice – and an essential part of the social contract that underlies medical research – that clinical trial data should be made publicly available less than one year after a clinical trial's completion. We strongly support WHO's effort to establish a global standard for reporting data within this timeframe, which is a practice we require of our grantees as well."

http://www.who.int/ictrp/results/jointstatement/en/
Registration and Reporting Requirements

Who is Responsible?

Responsible Party (RP) for a clinical trial must register the trial and submit results information. An RP can be:

- **Sponsor** of the clinical trial (as defined in 21 CFR 50.3) who initiates the study (i.e., “Johns Hopkins University”)
- **Principal Investigator** (PI)
- **Sponsor-Investigator** (the individual who both initiates and conducts the study)

Responsible Party is considered the Sponsor (“grantee organization for NIH-funded trials”)
Registration and Reporting Requirements

When to Register?

• ICMJE requires trial registry at or before first patient enrollment as a condition for publication

• Per FDAAA the Responsible Party for an Applicable Clinical Trial must submit required clinical trial information through the Protocol Registration and Reporting System (PRS) no later than 21 days after enrollment of the first participant.
  Source: https://www.clinicaltrials.gov/ct2/manage-recs/fdaaa
Updating the Record

More rapid updating is required for several data elements to help ensure that users of ClinicalTrials.gov have access to accurate, up-to-date information about important aspects of an applicable clinical trial or other clinical trial

The following data elements must be updated not later than 30 calendar days after a change occurs

- Study start date
- Intervention name(s)
- Availability of Expanded Access
- Expanded Access status
- Overall recruitment status
- Explanation for change in status
- Actual enrollment data
- Individual site status
- IRB status
- Completion Date
- Responsible Party
- Official Title
- Contact Information

5/11/2018
Update Requirements

When to update a study in-process?

- Each record must be reviewed for accuracy, and the Record Verification Date updated, at least every 12 months, even if there have been no changes to the study.
- The need to update ends when the study is completed or terminated and the results are entered, approved and posted.

Set calendar reminder to keep track of these deadlines. Don’t be like this…

Study Status

Record Verification: March 2017

⚠️ WARNING: A record for an active study (Overall Recruitment Status is not Completed, Terminated or Withdrawn) must be reviewed, updated and verified at least once per year.
Update Requirements

When to respond to comments?

• Registration and while Study is In-Process:
  – Must respond to PRS comments to correct errors, deficiencies and/or inconsistencies within 15 calendar days

• Results reporting:
  – Must respond to PRS comments to correct errors, deficiencies and/or inconsistencies within 25 calendar days
Reporting Requirements

When to Report Basic Results?

- No later than 12 months after (Primary) Completion Date.
- **Primary Completion Date** FDAAA [Required for records first released on or after December 1, 2008]
  - Date that the final subject was examined or recv’d an intervention for purposes of final data collection for the primary outcome, whether the trial concluded per protocol or was terminated.
  - Must keep this field accurate in clinicaltrials.gov since it’s how NIH determines the timeliness of basic results reporting.
- **Study Completion Date**
  - Final date on which data was (or is expected to be) collected.

Source: [https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryCompletionDate](https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryCompletionDate)
Reporting Requirements

When to submit Basic Results?

- **Study Start Date:**
  - **Month:** January
  - **Day:**
  - **Year:** 2014
  - **Type:** Actual
  - Beginning of participant enrollment.

- **Primary Completion Date:**
  - **Month:** June
  - **Day:**
  - **Year:** 2016
  - **Type:** Actual
  - Final data collection date for primary outcome measure.

- **Study Completion Date:**
  - **Month:** December
  - **Day:**
  - **Year:** 2016
  - **Type:** Actual
  - Final data collection date for study.
Practical Application

How long will it take to...

- Register a Trial? ClinicalTrials.gov estimates up to 10 hours
- Submit Basic Results? ClinicalTrials.gov estimates up to 50 hours
  - Highly variable based on study specifics
  - Tables cannot be copy/pasted from publication
  - May need statistical assistance
  - ClinicalTrials.gov will assist if needed
  - Plan to begin results entry 3 months prior to due date

### Table 3—Estimated Burden for Registration and Results Information Submission at ClinicalTrials.gov

<table>
<thead>
<tr>
<th>Type of respondents</th>
<th>Number of respondents</th>
<th>Frequency of response</th>
<th>Average time per response (hours)</th>
<th>Annual hour burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration</td>
<td>7,400</td>
<td>1 Initial</td>
<td>8</td>
<td>59,200</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 Subsequent Updates</td>
<td>2</td>
<td>118,400</td>
</tr>
<tr>
<td>Results Information</td>
<td>7,400</td>
<td>1 Initial</td>
<td>40</td>
<td>296,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 Subsequent Updates</td>
<td>10</td>
<td>148,000</td>
</tr>
<tr>
<td>Certifications to delay results submission</td>
<td>5,150</td>
<td>1</td>
<td>0.5</td>
<td>2,575</td>
</tr>
<tr>
<td>Extension requests and appeals</td>
<td>250</td>
<td>1</td>
<td>2</td>
<td>500</td>
</tr>
<tr>
<td>Registration triggered by voluntary submission.</td>
<td>88</td>
<td>1</td>
<td>8</td>
<td>704</td>
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<tr>
<td>Results triggered by voluntary submission</td>
<td>30</td>
<td>1</td>
<td>45</td>
<td>1,350</td>
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<tr>
<td>Expanded access records</td>
<td>213</td>
<td>1 Initial</td>
<td>2</td>
<td>426</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 Subsequent Updates</td>
<td>0.25</td>
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<tr>
<td>Subtotal for Regulated Submissions</td>
<td></td>
<td></td>
<td></td>
<td>627,262</td>
</tr>
</tbody>
</table>
Practical Application

How to Register

http://clinicaltrials.gov/ct2/manage-recs/how-register

1. Obtain a PRS user account, and know your institutional PRS account name
   – Each user should have their own account (no account sharing)
   – If you are leaving your position or the institution, make sure to transfer your responsibilities
Practical Application

2. Populate the Access List
   – Anyone who will need to view or modify the record
   – Only people with accounts will appear on the Access List
Practical Application

3. Enter the required and optional data elements

   **Outcome Example:**
   
   Title: “Pain severity as measured by the Visual Analog Scale (VAS)”
   
   Description: “Pain severity will be assessed using a VAS which ranges from 0 = “no pain” and 10 = “most severe pain.”
   
   Time frame: 2 weeks post-intervention
Practical Application

4. Preview, inspect and mark as Entry Complete
   - review the ClinicalTrials.gov Protocol Review Criteria document
Before you mark your record as complete you should…

Check for spelling and to see that all acronyms are expanded using the “Spelling” feature.

Possible Unexpanded Acronyms

Acronyms should be expanded at least the first time used in the Protocol section and (if applicable) in the Results section.

Example: National Institutes of Health (NIH)

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Acronym</th>
<th>Possible Expansion(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed Description</td>
<td>AI</td>
<td>[15]</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>DE</td>
<td>[8]</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>ID</td>
<td>[45]</td>
</tr>
<tr>
<td>Primary Outcome Measure</td>
<td>OFC</td>
<td>[3]</td>
</tr>
</tbody>
</table>
Registration: Tips and Tricks

Before you mark the record as complete you should...

- Check all Outcome Measures for accuracy and completion
- Check for any “Errors” or “Warnings”
Record Checklist for PRS Administrators

- Remove all personal pronouns. For example, change “I,” “we” and “our” to “the investigator(s) and “you” to “the participant(s).”
- Use the Spelling link at the top of the “Record Summary” page to correct spelling and locate and unexpanded acronyms. Expand all acronyms and abbreviations (and include acronym in parentheses) at least the first time use in both the Protocol and Results sections.
- Format inclusion/exclusion criteria in bullet format. Refrain from numbering.
- Remove parenthetical citations within the Protocol Section.
- Make sure that record verification is the current month.
- Ensure that the PI is the Record Owner. May need to add the previous Record Owner to the Access List.
- In the document section each document must include a cover page with the Official Title of the study, NCT number (if available), and date of the document. Ensure the date of the document is the same in both the document and the free test field.
- In Baseline Characteristics use the Measure Type “Count of Participants” instead of “Number”
Record Checklist for PRS Administrators

- Outcome Measures should be in the following format:
  - Title: Each outcome must assess one and only one variable and should specify the measurement that will be used (descriptive name of scale, physiological parameter, questionnaire) which will be used to assess the outcome.
    - Outcome title is not vague
    - Outcome does not describe multiple assessments
    - Outcome identifies the measurement to be used
  - Time Frame: Should be one specific time point at which the outcome is being assessed or which data will be presented (1 year, up to 12 months). The exception is, a change between TWO specific time points (i.e. baseline and 6 weeks).
  - Description: Should include details about the assessment tool, including, units of measure, score range, significance of score within the scale, and any other relevant details about procedure or assessment tool.
Top 10 Tips for Preventing Common Errors

1. Make sure the enrollment # in the protocol section does not conflict with the # of participants Started in the Participant Flow module

2. Use the Arm/Group Description to provide additional details about the interventions administered *(e.g., dosage, dosage form, frequency of administration) or groups evaluated.

3. Expand all acronyms and abbreviations the first time used (and include acronym in parentheses).

   Use “Spelling” feature

   **Possible Unexpanded Acronyms**

<table>
<thead>
<tr>
<th>Data Element</th>
<th>Acronym</th>
<th>Possible Expansion(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed Description</td>
<td>AI</td>
<td>[15]</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>DE</td>
<td>[8]</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>ID</td>
<td>[45]</td>
</tr>
<tr>
<td>Primary Outcome Measure</td>
<td>OFC</td>
<td>[3]</td>
</tr>
</tbody>
</table>
Top 10 Tips for Preventing Common Errors

4. Ensure the # of Participants analyzed is consistent with numbers provided in the Participant Flow Module. If not explain in the “Analysis Population Description”

5. The Outcome Measure Title describes WHAT was measured not WHY it was measured.

6. Each Outcome must assess only one variable. For example do not use “Weakness and fatigability.”

7. The Outcome Measure Description should specify HOW the outcome will be measured, including units and a detailed description of any scales and/or methodology used.

8. The Outcome Measure Time Frame should describe one time point unless assessing a change between two time points, time to event or pharmacokinetic measurements

9. In the Document Section, each document must include a cover page with the Official Title of the study, NCT number (if available), and date of the document.

10. Make sure all previous comments have been addressed.
Helpful Links

• How to Submit Your Results homepage  

• Basic Results Data Elements Definitions  
  http://prsinfo.clinicaltrials.gov/results_definitions.html

• 10 minute webinars for each results module  
  http://clinicaltrials.gov/ct2/manage-recs/present

• Helpful Hints (with common study designs examples)  
  http://prsinfo.clinicaltrials.gov/ResultsExamples.pdf

• ClinicalTrials.gov Review of Protocol Submissions  
  http://prsinfo.clinicaltrials.gov/fdaaa.html
Clinical Trials Registration and Results Reporting Taskforce

The Clinical Trials Registration and Results Reporting Taskforce is a national consortium of members of academic medical centers, universities, and hospitals focused on the implementation of domestic clinical trials registration and results reporting requirements in the ClinicalTrials.gov public repository. The objectives of the group are to identify best practices, develop solutions and tools for regulatory support and investigators, and serve as a communication forum.

How to Join
Interested in joining the Taskforce?
Read more at our Membership webpage!

Next Meeting
Our next Taskforce meeting is scheduled for Thursday, April 19, 2018 from 1-2pm EST.
Clinical Trials Registration and Results Taskforce

Membership:
Academic institutions
• Started as a Taskforce of the CTSA consortium
• Taskforce members are institutional resources responsible for oversight and administration of ClinicalTrials.gov registration and results reporting

Focus:
Domestic clinical trials registration and results reporting requirements

Objectives:
• Identify best practices
• Develop tools for regulatory support and investigators
• Serve as a communication forum

Next call
May 17th
1:00pm EST

5/11/2018
https://ctrrtaskforce.com/
Taskforce –
Member Institutions (111)

A.T. Still University
Albert Einstein College of Medicine
Association of American Medical Colleges
Baptist Health
Baylor College of Medicine
Beaumont Health
Boston Medical Center
Boston University
Brown University
Buffalo University
Cambridge Health Alliance
Cancer Treatment Centers & Hospitals
Cedars-Sinai Medical Center
Children’s Healthcare of Atlanta
Children’s Hospital of Philadelphia
Children’s National Health System
Cleveland Clinic
Columbia University Medical School
Dartmouth Hitchcock Medical
Dartmouth University
Duke University
Emory University
Fenway Health
Fred Hutchinson Cancer Research Center
George Mason
Georgetown University
Harvard
Houston Methodist
Huntsman Cancer Institute, University of Utah
Icahn School of Medicine at Mount Sinai
Indiana University
John Hopkins Medical Institutions
John Hopkins University
Kennedy Krieger Institute
Mayo Clinic
MD Anderson
Medical University of South Carolina
Miami Children’s Hospital
Moffit Cancer Center
National Institute of Health
 Nationwide Children’s Hospital
Northwestern University
NYU Langone Health
Ochsner Health System
Ohio State Wexner Medical Center
Oregon Health and Science University
Palmetto Health
Partners Healthcare
Penn State Health
Pennsylvania State University
Princeton University
Public Responsibility in Medicine and Research
Radford University
Rockefeller University
Roger Williams Medical Center
Rutgers University
Saint Louis University
Stanford University
State University of New York College of Optometry
Texas Tech University Health Sciences Center
Tufts Medical Center
UC Davis Health
University of Connecticut Health
University of Texas Southwestern
University of Alabama Medical School
University of California at Davis
University of California at San Francisco
University of California Los Angeles
University of California, Irvine
University of California, San Diego
University of Chicago
University of Cincinnati
University of Colorado Denver
University of Florida
University of Illinois at Chicago
University of Iowa
University of Kansas Medical Center
University of Kentucky
University of Louisville
University of Maryland
University of Miami
University of Michigan
University of Michigan Medical School
University of North Carolina
University of North Carolina Medical School
University of Notre Dame
University of Oklahoma Health Sciences Center
University of Pennsylvania
University of Pennsylvania Medical School
University of Pittsburgh
University of Pittsburgh Medical Center
University of Rhode Island
University of Rochester Medical School
University of South Alabama
University of South Florida
University of Texas Health San Antonio
University of Texas Medical Branch
University of Utah
University of Vermont
University of Virginia School of Medicine
University of Wisconsin
UT Health Science Center Houston
Vanderbilt University
Vanderbilt University Medical Center
Veterans Administration
Virginia Commonwealth University
Virginia Commonwealth University Health
Wake Forest Baptist Health
Washington University in St. Louis
Weill Cornell Medicine
Yale University
How to become a Taskforce member?

If you are interested in becoming a Taskforce member, please fill out the online request form.
Clinical Trials Registration and Results Taskforce

• Administration and oversight quantitative survey [Accepted for publication (BMC Medicine)]
• Template presentation slides (registration & results reporting)
• Template questions to identify Applicable Clinical Trials (in eIRB application)
• Qualitative survey of organizational policy
• Guidance on how to manage relocation of the Responsible Party
• NIH dissemination plans and ICMJE data sharing statements
• Sample job descriptions
• Sample Policies and SOPs
• Considerations for protocol redaction prior to posting
• Forum for feedback to ClinicalTrials.gov staff

If you are interested in hearing more about the Taskforce please visit https://ctrrtaskforce.com/
Thank you!

Thank you for your time and attention

If you have further questions you can reach me at registerclinicaltrials@jhmi.edu
NIH Policy Sample Language – Example 1

Dissemination of study results through ClinicalTrials.gov registration and reporting at a minimum will include the following components:

• X (insert name or role, can be a designee) will be responsible for handling ClinicalTrials.gov requirements for this project under the PI’s oversight. S/he will register the trial prior to enrolling the first subject. Once a record is established, s/he will confirm accuracy of record content; resolve problems; and maintain records including content update and modifications. S/he will also be responsible for aggregate results reporting and AE reporting at the conclusion of the project.

• Add specifics related to this trial.

Courtesy of Sarah White (Harvard)
NIH Policy Sample Language – Example 2

• As applicant for this award, I will ensure that clinical trials under the award are registered and results information is submitted to ClinicalTrials.gov as outlined in the policy and according to the specific timelines stated in the policy. Registration will occur no later than 21 days following enrollment of the first subject. Once a study record is established, required updates will be performed at least once every 12 months, or more frequently as required, confirming the completeness and accuracy of the study record. Summary results will be submitted by the standard results submission due date, and any required results updates will be submitted within the time frames specified in the ClinicalTrials.gov regulations.

• The sponsor institution has an internal policy in place to ensure that clinical trials registration and results reporting occur in compliance with requirements contained in NIH Policy on the Dissemination of Clinical Trial Information (NOT-OD-16-149).

• Informed consent documents for this clinical trial will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov.

Courtesy of Scott Patton (Stanford)
Select References

- ACT Wizard: http://grants.nih.gov/clinicaltrials_fdaaa/docs/Flow_chart-ACT_only.pdf
- Clinicaltrials.gov history: https://www.clinicaltrials.gov/ct2/about-site/history
- Clinicaltrials.gov homepage: https://www.clinicaltrials.gov/
- Clinicaltrials.gov FAQ: https://clinicaltrials.gov/ct2/manage-recs/faq
- FDA Guidance on Form FDA 3674: http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm
- HHS takes steps to provide more information about clinical trials to the public https://www.nih.gov/news-events/news-releases/hhs-takes-steps-provide-more-information-about-clinical-trials-public
Select References – Final Rule

- Federal Register Notice: HHS Final Rule
- Federal Register Vol. 81, No 183, September 21, 2016
- Federal Register Notice: NIH Policy
- Summary Table: HHS Final Rule and NIH Policy
- Summary of Changes: HHS Final Rule and NIH Policy
- JAMA: Toward a New Era of Trust and Transparency in Clinical Trials
- NEJM: The Final Rule for US Clinical Trial Registration and Results Information Submission
- NIH Director’s Blog: Clinical Trials – Sharing of Data and Living Up to Our End of the Bargain
- NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information
Select References – NIH Definition of Clinical Trial

- **Case Studies** (These simplified case studies illustrate the differences between clinical trials and clinical studies)
- **Decision Tree**
- **FAQs** (These FAQs further clarify the application of the clinical trial definition)
- **NOT-OD-15-015** Notice of Revised NIH Definition of “Clinical Trial” (Released 10/23/14)
Select Publications


• Gopal AD, Desai NR, Tse T, Ross JS. Reporting of noninferiority trials in ClinicalTrials.gov and corresponding publications. JAMA. 2015 Mar 17;313(11):1163-


• Zarin DA, Keselman A. Registering a clinical trial in ClinicalTrials.gov. Chest. 2007;131(3):909-12

