ClinicalTrials.gov

42 CFR PART 11
AND

NIH POLICY ON THE DISSEMINATION OF
NIH-FUNDED CLINICAL TRIAL INFORMATION

Clinical Research Quality, Spectrum

SMART Meeting
December 13, 2016

Overview

- Introduce Clinical Research Quality
- ClinicalTrials.gov Update
  - New regulations – effective January 18, 2017
  - New NIH policy – effective January 18, 2017
  - NIH long-term plan
- Roles and Responsibilities
  - Which studies?
    - Applicable Clinical Trials
    - NIH-funded Clinical Trials (NIH-definition)
  - Who’s responsible?
- How is Stanford responding?
  - School of Medicine policy
  - eProtocol changes
  - CRQ team support
Clinical Research Quality (CRQ) – Spectrum

- **New School of Medicine Venture**
- **Facilitate** clinical research regulatory compliance
- Develop standard operating procedures and guidance for the SoM, align with departmental and program/institute standard operating procedures (SOPs)
- Education and training
- Quality audits of clinical research
- Assist with corrective and preventive action (CAPA) plans
- Recommend reporting
- Collaborate with Stanford University Research Compliance Office

- Quality Improvement team
- Clinical Trial Disclosure team – ClinicalTrials.gov

Clinical Research Quality (CRQ) website

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ClinicalTrials.gov Study Registration and Results Reporting

- Regulation 42 CFR 11 requires registration and results reporting of Applicable Clinical Trials (ACTs)
  - Interventional trials of drugs/biologics (other than Phase 1) and devices (other than small device feasibility studies) conducted in the U.S. or under an FDA IND/IDE

- NIH Policy #NOT-OD-16-149 requires registration and results reporting of all NIH-Funded clinical trials (NIH-CTs) regardless of phase or intervention type ¹
  - Studies that use NIH-funded infrastructure but do not receive other NIH funding are not in scope

- Voluntary registration and results reporting is allowed for any clinical study
  - Can be registration only, or registration plus results reporting

- ICMJE policy requires study registration as a prerequisite for publication ²

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Regulations + NIH Policy: Increased Scope for CTgov Registration and Results

NIH-funded Clinical Trials *

Newly in scope

Applicable clinical trials (ACTs)

Already in scope per FDAAA (now per Regulations)

NIH-funded Clinical Research

Non-NIH-funded Clinical Research

* NIH Clinical Trial Definition (October 23, 2014): A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

NIH Clinical Trial Quality Initiatives

Multi-faceted Effort to Improve Quality and Efficacy of Clinical Trials

- Protocol template will help ensure that investigators prepare protocols that contain all the information necessary to enable efficient and timely review by institutional review boards (IRBs) and to be in compliance with FDA IND application regulations (Notice #NOT-OD-16-043)

- NIH has adopted a policy for using a single IRB of record for the review of NIH multisite studies and has developed standardized agreements that will allow institutions to rely on a single IRB of record (Notice #NOT-OD-16-094)

- New NIH policy requires all applications for clinical trials to be submitted in response to clinical trial-specific Funding Opportunity Announcements (FOAs) (Notice #NOT-OD-16-147)

- NIH will require Good Clinical Practice (GCP) training for investigators and NIH staff responsible for conducting or overseeing clinical trials (Notice #NOT-OD-16-148)

- NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (Notice #NOT-OD-16-149)

Hudson et al., JAMA. Oct 4, 2016; 316(13):1353-1354

Stanford University
Figure. Improving Clinical Trials. The new, multifaceted effort shown above will enhance the quality and efficiency of NIH-supported clinical trials by focusing on a variety of key points along the "lifespan" of a clinical trial.

NIH Vision of the Clinical Trial Life Cycle

Provisions for Enforcement

- Enforcement mechanisms provided in the Regulations & NIH Policy

<table>
<thead>
<tr>
<th>Reporting Requirement</th>
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<tr>
<td>Scope</td>
<td>Registration</td>
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<td>Registration and Results Reporting</td>
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<tr>
<td>Phase</td>
<td>All</td>
<td>Not phase 1 (drugs/biologics) Not feasibility (devices)</td>
<td>All</td>
</tr>
<tr>
<td>Intervention Type</td>
<td>All</td>
<td>Drugs, Biologics, and Devices regulated by the FDA</td>
<td>All (e.g., including behavioral interventions)</td>
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<td>Funding Source</td>
<td>Any</td>
<td>Any</td>
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<td>Enforcement</td>
<td>Refusal to publish</td>
<td>Criminal proceedings and civil penalties (up to $10,000/day); loss of HHS funding</td>
<td>Loss of NIH funding</td>
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NIH Webinar 1 (September 27, 2016); ICMJE: International Committee of Medical Journal Editors; http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
School of Medicine Policy

- Any Stanford researcher, in the role of principal investigator or protocol director, who initiates or conducts an investigator-initiated clinical trial, shall be designated as the Responsible Party (RP). […]
- Registration must be done via Stanford’s account in the Protocol Registration and Results System (PRS), […] unless the project receives external funding that is administered by another institution (e.g., PAVIR).
- Trials that have allocated patient care charges to be billed to Medicare or other third-party payers must provide an NCT# to Stanford Health Care Patient Financial Services to avoid payer denials.
- The IRB eProtocol system will require ClinicalTrials.gov registration and assignment of an NCT# for all ACTs and NIH-CTs prior to IRB submission.
- Noncompliance with the regulations or NIH policy to submit results for an ACT or NIH-CT (in general, no later than 12 months after the Primary Completion Date), or repeated violations of the regulations, NIH policy, or this policy, can result in administrative action by School of Medicine or department leadership, such as reduction of incentive bonus payments, or withdrawal of further research privileges.

Support for CTgov Tracking and Compliance

- School of Medicine
  - Dean Minor emphasizing departments must bring existing CTgov study records into compliance
  - New School of Medicine policy
  - Dedicated staff in Spectrum/CRQ office (2.5 FTEs)
  - Collaboration between RMG & Spectrum/CRQ
    - Reports to departments
    - NIH policy
    - Collaboration with IRB

- Department & Program Support
  - Administrator Working Group to support efforts in large departments
  - CCTO, SCCR alignment
Resources – NIH Policy

- NIH News Release on the HHS Regulations and NIH Policy

- NIH Policy on the Dissemination of Clinical Trial Information

- Questions: clinicaltrials.disseminationpolicy@mail.nih.gov

Resources: CTgov/Regulations

- CTgov
  > Protocol (registration) element definitions
    > https://register.clinicaltrials.gov/prs/html/definitions.html
  > Results element definitions

- Regulations
  > General submission information: https://clinicaltrials.gov/ct2/manage-recs
  > Changes from Current Practice Described in the Regulations (PDF)
  > General information on Regulations: https://prsinfo.clinicaltrials.gov

- Questions: register@clinicaltrials.gov
Contact Us

- CRQ CTgov team: Elaine Basaca, Scott Patton, or Jennifer Brown
  > clinicaltrials-gov@stanford.edu

- For cancer studies, contact the Cancer Clinical Trial Office (CCTO)
  > Sarah Pelta- General submissions CCTO-Website@stanford.edu
  > Neal Birkett- Results Reporting nbirkett@stanford.edu

- Department administrative support
  > Medicine/SCCR
  > Psychiatry and Behavioral Sciences
  > Anesthesia
  > Pediatrics
  > Radiology
  > Neurology/Neurosurgery