2019 SRAI Annual Meeting
October 19-23

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Navigating the Organizational Impact of Recent Changes in Federal Regulation & Policy
Navigating Change – U.S. Rules

• Revised Common Rule
• 21st Century Cures Act
• Certificates of Confidentiality
• Single IRB Mandates
• Digital Health – Definition of Medical Device
• Expanded Access and Right to Try
• Genomic Data Sharing

• Definition of Clinical Trial
• GCP Training
• Posting of Clinical Trial Consent Forms
• Definition of Clinical Trial
• Concept of Identifiability
• Inclusion Policies
• Clinical Trials Registration & Reporting of Results
• Humanitarian Use Devices
Certificates of Confidentiality

- **21st Century Cures mandate – 42 U.S.C. 241**
  - Federal funding = automatic issuance (currently NIH, CDC, FDA)
  - Burden on institutions & investigators to determine applicability
- Shifted focus away from sensitivity to potential identifiability
- Concept of identifiability –
  - “at least a very small risk” vs. Common Rule “could readily be ascertained”
- Consent required for disclosures (including for medical treatment)
  - Exceptions – disclosures required by law (e.g., communicable diseases) & for “other scientific research” that complies with human subject regulations
- Information protected “for perpetuity”
- Internal controls & downstream notification requirements
- NIH & CDC – individual level genomic data is covered
- Other Confidentiality Statutes (e.g., AHRQ, NIJ) vs. CoC
Challenges

• Responsibility for determining if a CoC applies
  • Not all covered research will be subject to IRB review
  • Secondary use of research data and knowing if it is covered by a CoC (e.g., NIH repositories such as dbGaP have CoCs)

• Consent for disclosures (e.g., inclusion of trial information and copies of consent forms in medical records)

• Ensuring that all persons with access to covered information understand restrictions and responsibilities

• Managing downstream notifications

• Staying informed (e.g., which agencies are “automatically issuing” vs. need to apply)

• Responding to information demands, lack of physical certificate
Certificates of Confidentiality

Discussion
Single IRB Mandate – NIH Policy

• NIH Policy
  • Applies to all domestic sites participating in multi-site studies where each site is conducting the same protocol
  • Does not apply to career development, research training or fellowship awards
  • Does not apply to exempt research
  • Exceptions –
    • Existing federal, state, or tribal law, regulation, or policy
    • Compelling justification
Single IRB Mandate – Revised Common Rule

• Compliance date - January 20, 2020

• Applies to:
  • Research subject to the revised Common Rule
  • “Any institution located in the U.S. that is engaged in cooperative research...for that portion of the research that is conducted in the U.S.”
  • “Cooperative research are those projects...that involve more than one institution.”

• Does not apply when:
  • More than single IRB review is required by law (including tribal law)
  • The Federal dept or agency supporting or conducting the research determines that single IRB is not appropriate
Challenges

• Revised Common Rule provision applies to all cooperative studies that are subject to the revised Rule including existing studies that were -
  • IRB-approved on or after Jan. 21, 2019
  • Voluntarily transitioned to comply with the revised Rule

• Scope of rule is broader than NIH policy scope but also encompasses NIH studies

• Lack of revised Common Rule guidance
Challenges

• NIH policy requires sIRB plan at grant application
• Requests for exceptions have to be included in the grant application
• Forces acceptance of IRBs that organization might not be comfortable with or loss of grant opportunity
• Costing sIRB
• “Last-minute” nature of grants
Challenges

• Managing reliance agreements
• Managing division of responsibilities
• Managing local context and local requirements
• Management and communication of important information and issues
• Maintaining local knowledge and oversight of ceded studies
Single IRB Mandates

Discussion
Clinical Trial Definition

Revised Common Rule Definition:

• Clinical trial means 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 the interventions on biomedical or behavioral health-related outcomes

Triggers:

• Requirement for posting one IRB-approved informed consent form used to enroll subjects on a publicly available Federal web site after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject
Clinical Trial Definition

NIH Definition:

- 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
- **Intervention examples** - drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies
Clinical Trial Definition

NIH (continued)

Triggers:

• FOA restrictions (clinical trial not allowed, clinical trial required, etc.)
• Application requirement - Human Subjects and Clinical Trials Information Form
• Specific review criteria for clinical trials by award type
• Clinical trials registration (Clinicaltrials.gov)
  • No later than 21 days after enrolling the first subject
  • Update record at least once every 12 months
  • Post summary results no later than 1 year after clinical trial completion
  • Notice of registration in informed consent forms
• GCP training requirement
Clinical Trial Definition

ICMJE Definition:

• Any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the relationship between a health-related intervention and a health outcome

• Intervention examples - drugs, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes

Triggers:

• Requirement for registration of study in a WHO ICTRP registry or Clinicaltrials.gov at or before the time of 1st enrollment

• Inclusion of data sharing plan in the registration

• Inclusion of data sharing statement in manuscripts
Clinical Trial Definition

WHO Definition:

• Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

• Intervention examples - drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments, process-of-care changes, preventive care, etc.
Clinical Trial Definition

WHO (continued)

Triggers (WHO Resolution):

• Clinical trial registration in a WHO ICTRP registry or ICMJE-approved registry before the 1st subject receives the first medical intervention
• Registration must be updated to include final enrollment numbers and completion date
• Key outcomes must be posted within 12 months of study completion
• Main findings must be submitted for publication in a peer reviewed journal within 12 months of completion and published through an open access mechanism or otherwise made publicly available within 24 months
• Inclusion of trial ID in publications and PubMed abstract
Clinical Trial Definition

FDAAA 801:

- Applicable clinical trials are (1) clinical trials of drug and biological products that are controlled, clinical investigations, other than phase 1 investigations, of a product subject to FDA regulation; and (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies); or (3) any pediatric post-market surveillance studies required by FDA under the FD&C Act.
Clinical Trial Definition

FDAAA 801 (continued)

Triggers:

• Requirement for registration in Clinicaltrials.gov no later than 21 days after enrollment of the 1st participant
• Submission of results information no later than 1 year after the date of final data collection for the primary outcome measure (delay exceptions permitted under certain circumstances (marketing approval or clearance is being sought)
• Clinicaltrials.gov compliance certification for drug, biologics, and device submissions to the FDA
• Notice of registration in informed consent forms
Challenges

- Multiple definitions encompassing much more research than conventional “clinical trials”
  - GCP training for SBER research
  - Appropriate registration and reporting of basic research that also meets definition of clinical trial
- Wide variance in requirements for registration & posting of results
- Knowing which standards you have to comply with at onset or risk of publication being rejected
- Educating research community, ensuring compliance
Clinical Trials Definition

Discussion
Genomic Data Sharing

• NIH GDS Policy applies to
  • All NIH-funded research (basic and clinical) that generates large-scale human or non-human genomic data, as well as the use of these data for subsequent research
  • Includes use of genomic data obtained from NIH-designated repositories such as dbGaP
Genomic Data Sharing

Requirements -

• A genomic data sharing plan must be submitted with the funding application
• Institutional Certification must be submitted with Just-in-Time Information
• Consent must be obtained for broad data sharing on an opt-in basis, participants cannot be disqualified if they decline unless data sharing is intrinsic to the purpose (e.g., the purpose is to establish a repository for future research)
• Expectations and timelines for data submission and release are dependent on the type of data (human vs. non-human) and the level of data processing that is needed before submission.
  • For human data, generally - submission within 3 months of data generation, and release up to 6 months after submission or at the time of acceptance of initial publication (whichever occurs first).
Genomic Data Sharing

• Institutional Certification
  • “Institutional Signing Official” – senior official credentialed through ERA Commons & authorized to enter institution into a legally binding contract
  • Certification must be provided for all sites contributing samples. Alternatively, the primary site may submit on behalf of all contributing sites (responsible for gathering necessary information from all sites)
Genomic Data Sharing

Institutional Certification

- Submission is consistent with applicable laws, regulations, and policies
- Any limitations on the use of the data expressed in the informed consent documents are included with the certification
- Individual identities will not be released to the repository
- IRB or Privacy Board review of data submission proposal with 5 specific assurances
- Designation of individual-level data as controlled access or unrestricted access
- Designation of Genomic Summary Results
Genomic Data Sharing

• The requirements for informed consent and for Institutional Certification also apply to data voluntarily submitted to dbGap
• Data in NIH-designated repositories (such as dbGaP) is protected by a Certificate of Confidentiality thus protected for perpetuity
Challenges

- Certification at just-in-time but must attest to consistency with consent form that is likely not approved yet
- Designation as controlled vs. uncontrolled, identifying data use limitations at just-in-time
- Management of certifications for multi-site research
- Ensuring upfront compliance with consent and other requirements when registration is voluntary
- Tracking and managing opt-outs
- Managing secondary use of CoC-protected data
Genomic Data Sharing

Discussion
Revised Common Rule

• Effective January 2019
• Major revisions including:
  • New type of review – exempt with limited IRB review
  • Broadened exemptions
  • Elimination of continuing review for much research
  • Reliance agreement/procedure requirements
  • Introduced liability for external IRBs
  • Added requirement for IRBs to ensure investigator compliance
Revised Common Rule

• Major revisions (continued):
  • New & revised consent requirements – process & elements
  • New criterion for waivers of consent
  • Introduction of broad consent option

• Pending:
  • Reconsideration of “identifiability”
  • Revised expedited categories
  • Revised FWA and IRB registration
  • Single IRB mandate
Challenges

- Lack of promised guidance
- Unwieldy requirements
- Management of multiple, conflicting “rules”
  - Studies subject to prior Common Rule (pre-2018 requirements)
  - Studies subject to revised Common Rule
  - Dept of Justice – not a signatory, must continue to apply pre-2018 requirements and document accordingly
  - Studies subject to both Common Rule and FDA
Challenges

- Unanticipated issues such as
  - FWA + State Law
  - HHS requirements for review of guidance
  - Widespread rejection of broad consent
  - Limitations associated with HIPAA exemptions
  - Lessons learned from NIH sIRB mandate
- Single IRB and pre-existing studies
- Increased administrative burden
Genomic Data Sharing

Discussion
Navigating the Organizational Impact of Change

Questions?

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