“Hot” Topics in Human Subjects Research

Office of Responsible Research Practices
July 17, 2018
Session Objectives

• Present regulatory updates
• Explain Ohio State’s implementation of recent human subjects research changes
• Review best practices and available resources
Session Overview

- Revised Common Rule
- dbGaP
- Privacy vs. Confidentiality
- Certificates of Confidentiality
- Q&A
Session Overview

- Revised Common Rule
- dbGaP
- Privacy vs. Confidentiality
- Certificates of Confidentiality
- Q&A
Major Common Rule Revisions

- Definitions
- Exemptions
- Informed Consent
- Continuing Review
- Single IRB
Definitions
Revised Definitions

**Human subject:** a living individual about whom an investigator conducting research

- Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
- Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable bio-specimens
Research: Four categories of activities were removed from the definition to make clear that they are NOT within the Rule’s jurisdiction:

- Scholarly or journalistic activities that focus directly on specific individuals
- Public health surveillance activities
- Authorized operational activities for national security missions
- Data collection/analysis activities carried out as part of the criminal justice system
New Definition

**Clinical Trial:** 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.
Exemptions
Exemption Changes

Pre-2018 Rule

• Exemption 1
• Exemption 2
• Exemption 3
• Exemption 4
• Exemption 5
• Exemption 6

Revised Common Rule

Restrictions added
Expanded*
Removed and replaced with a new exemption 3*
Expanded old and added new
Expanded with changes
No change
New Exemption 7*
New Exemption 8*

*New - limited IRB review
Limited IRB Review

- Required for exemptions 2, 3, 7, and 8 in the revised Common Rule
- Expedited review can be used
- One time only, no continuing review required
  - **Exemptions 2 and 3** review:
    - For privacy and confidentiality protection
  - **Exemptions 7 and 8** review:
    - For other safeguards related to privacy and confidentiality protection, and **broad consent**
Exemption 1: *Restrictions Added*

Normal educational practices in established or commonly accepted educational settings

- What’s new?

Normal educational practices that are not likely to adversely impact:

- Students’ opportunity to learn required educational content, or
- The assessment of educators who provide instruction
Exemption 2: *Expanded*

Research that *only* includes interactions involving educational tests, surveys, interviews, and observations of public behavior when:

- Information recorded cannot be readily linked back to subjects, *or*
- Any information disclosure would not place subjects at risk of certain harms (including to educational advancement), *or*
- Identifiable information recorded, and IRB conducts **limited IRB review** for privacy and confidentiality protection under §_.111(a)(7)
What Happened to Exemption 3?

Removed in revised Common Rule

• Pertained to research involving the use of educational tests, survey procedures, or observation of public behavior if:
  • The human subjects are elected or appointed public officials or candidates for public office, or
  • Federal statute requires protection of confidentiality without exception.

• Most would be exempt under the new exemption 2. If recording sensitive, identifiable information about public officials, it must be kept confidential.
Exemption 3: New

Research involving benign behavioral interventions with adults who prospectively agree when information collection is limited to verbal or written responses (including data entry) or audiovisual recording, and:

- Information recorded cannot be readily linked back to subjects, or
- Any information disclosure would not place subjects at risk of certain harms, or
- Identifiable information recorded, and IRB conducts limited IRB review for privacy and confidentiality protection
Exemption 3 (cont.)

- Benign behavioral interventions:
  - Brief in duration
  - Harmless, painless, not physically invasive
  - Significant adverse lasting impact unlikely
  - No reason to think subjects will find interventions offensive or embarrassing

- Includes *authorized* deception research
Exemption 4: *Expanded*

(Expanded options for secondary research)

**Secondary research**: re-using identifiable information and identifiable biospecimens that are collected for some other ‘primary’ or ‘initial’ activity. Does not cover primary collection of either information or biospecimens.
Exemption 4 (cont.)

- Information or biospecimens no longer must be “existing” at the time of the exemption determination.

- Certain research use of identifiable information may be considered exempt from the Final Rule if such data are subject to HIPAA protections.
Exemption 5: *Expanded*

Public benefit and service programs research and demonstration projects

- Expanded to apply to such Federally-supported research (no longer limited to Federally-conducted research)
- Added requirement that Federal agency publish a list of projects covered by this exemption prior to commencing the research
Informed Consent
Key Revisions

**New process requirements** for the content, organization, and presentation of information and the process to facilitate a prospective subject’s decision about whether to participate in research.

**New requirements** for the basic and additional elements of consent.

**New requirement to post**, to a federal website, a copy of an IRB-approved version of the consent form that was used for enrollment purposes for each clinical trial conducted or supported by a federal department or agency.
New process requirements

Promote Autonomy

Changes are intended to make informed consent more meaningful so that research subjects will have the necessary information to make informed decisions.

Information presented in sufficient detail, and organized and presented in a way that facilitates subject’s understanding of reasons why one might or might not want to participate in the research.
New process requirements (cont.)

The revised Rule requires that “key information” must receive priority by appearing at the beginning of the consent form and is presented first in the consent discussion

• The first section must provide a concise and focused presentation and not merely lists of isolated facts
Basic Element of Informed Consent

One new element:
Notice about possible future research use of information or bio-specimens stripped of identifiers:

- Notifying prospective subject that subjects’ information or bio-specimens could be used for future research without additional consent; or
- Notifying prospective subject that subjects’ information or bio-specimens will not be used for future research.
**Additional Elements of Informed Consent**

Three new additional elements (“when appropriate”):

- Notice about whether clinically relevant research results, including individual research results, will be given to subjects, and if so, under what conditions.
- Notice about possible commercial profit, and whether subjects will share in this profit (for research involving bio-specimens).
- Notice about whether research might include whole genome sequencing (for research involving bio-specimens).
Posting Consent Forms for Clinical Trials

For clinical trials supported by federal funding, one IRB-approved consent form used to enroll participants must be posted on publicly available Federal website (to be determined).

Post after recruitment closes, no later than 60 days after last study visit.

Federal department or agency may permit or require redactions.
Continuing Review
Continuing Review at Ohio State

Annual Status Report (ASR) format permitted for following study types:

- All minimal risk research (except FDA-regulated)
- *Federal funding no longer impacts ASR*

Continuing Review (CR) required for following study types:

- Greater than minimal risk research
- All FDA-regulated research

IRB has the ability to require CR for any study
Continuing Review at Ohio State

Maintain expiration dates

Final study reports required — added to CR and ASR submission forms

Permanent termination within 60 days if no CR/ASR submitted
Continuing Review Transition
Accrual Ongoing

<table>
<thead>
<tr>
<th>ASR Review</th>
<th>Federally Funded Minimal Risk</th>
<th>FDA/Greater than Minimal Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Trigger notice</td>
<td>• Trigger notice</td>
<td>• Consent amendment during CR</td>
</tr>
<tr>
<td>• Consent amendment</td>
<td>• Consent amendment</td>
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<tr>
<td>• Continue ASR</td>
<td>• Begin ASR</td>
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# Continuing Review Transition

## Accrual Complete

<table>
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</table>
| • Continue ASR  
  • Update consent with future ICF amendments | • Begin ASR  
  • Update consent with future ICF amendments | • Continue CR  
  • Update consent with future ICF amendments |
Single IRB

Final Rule implementation date:

January 20, 2020

NIH Single IRB effective date:

January 25, 2018
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Topic Overview

• dbGaP background
• Initial submissions
• Active studies
• Closed studies
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What is dbGaP?

- Database of Genotypes and Phenotypes (dbGaP)
- Archive and distribute genetic data and results
- Other NIH genomic data repositories
  - Gene Expression Omnibus
  - Sequence Read Archive
  - GenBank

- NIH requires:
  - IRB review
  - Institutional certification
Institutional Certification

Looks like this:

[Image of Institutional Certification form]
IRB Review

Looks like this:
Genomic Data Submission

• NIH-funded research
• Large-scale human or non-human genomic data
Topic Overview

• dbGaP background
• **Initial submissions**
• Active studies
• Closed studies
Initial Submissions

- Plan to submit genomic data
- Research protocol
- Consent document
- Institutional certificate
Research Protocol

• Intent to contribute data
• Specific sources of the data to be submitted
• Genotypic data
• Phenotypic data
• Any proposed restrictions for access
Research Protocol (cont.)

- Plan for removing identifiers
- No PHI included
- Multi-site studies
  - Specify scope of certification
  - Confirm collaborators’ agreement with single certification
Consent Document

- Study-related materials will be submitted to public, scientific databases
- Address future research use and broad data sharing
- Data provided are coded
- Data may be withdrawn
Institutional Certificate

• Complete through PI signature
• Fully executed copy returned with IRB approval
Topic Overview

- dbGaP background
- Initial submissions
- **Active studies**
- Closed studies
Active Studies

Amendment submission required

• Data proposal
• Revised protocol
• All consent versions
• Revised consent document (if accruing)
• Institutional Certificate
Active Studies
IRB determines:
• Data proposal consistent with:
  • Protocol
  • All consent form versions
• Data proposal inconsistent/requests:
  • Consent revision
  • Contact/re-consent of subjects
  • Additional information
• Data submission request denied
Topic Overview

- dbGaP background
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- Active studies
- **Closed studies**
Closed Studies

- Amendments are not possible
- Submit data-sharing requests to ORRP
- Provide relevant materials
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Definitions

Privacy
• Person
• Free from intrusion, observation

Confidentiality
• Identifiable information
• Protection from disclosure
Considerations

Privacy

- Control over sharing themselves
- Depends on the individual
- Accessing identifiable information
  - Original purpose
  - Sensitivity/risk from disclosure
  - Identifiable information required?
Considerations (cont.)

Confidentiality
- Identifiable information
- Informed consent description
  - Possible/planned sharing
  - Measures to protect information
Privacy of Participants

It is important to note the distinction between "privacy" and "confidentiality." In general, privacy concerns are about the people involved in the research (a person's desire to control the access of others to themselves), whereas confidentiality is associated with a participant's data collected for research purposes. This section should specifically address provisions to protect participants' privacy interests (e.g., limiting the number of people screening private records for recruitment, any interactions will be conducted in a way to avoid being witnessed or overheard, sensitive or medical information will be discussed in a private setting, etc.). For more information, please see the policy Privacy and Confidentiality.

All fields marked with an * are required.

Describe the provisions to protect the privacy interests of the participants.*

Consider the circumstances and nature of information to be obtained, taking into account factors (e.g., age, gender, ethnicity, education level, etc.) that may influence participants’ expectations of privacy.

You have entered 0 of 3000 characters.

Does the research require access to personally identifiable, private information?*

Yes  No

Describe the personally identifiable private information involved in the research.

List the information source(s) (e.g., educational records, surveys, medical records, etc.)*
Privacy Provisions

• Clinical team accessing information
• Clinical team introducing study
• Private setting
• Potential participants initiate contact
Explain how information is handled, including storage, security measures (as necessary), and who will have access to the information. Include both electronic and hard copy records.
Confidentiality Measures

- Pseudonyms in transcriptions
- Physical security of hard copies
- Cyber security of electronic copies
  - Secure servers
  - Password protection
  - Encrypted portable devices
- Data storage/handling arrangements
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Regulatory Changes

• 21st Century Cures Act
• Policy effective October 1, 2017
• Applies to NIH-funded research that was active on December 13, 2016 or subsequently approved
• Automatically issued for studies collecting and/or using sensitive, identifiable information
Subject identified

“Covered information”

“Very small” risk of re-identification

Individual level human genomic data
Recipient Responsibilities

• No disclosure in proceedings w/o consent
• No disclosure outside of research team
• Inform other recipients of restrictions
• Exceptions
  • Required by law
  • Medical treatment
  • Consent of subject
  • Other scientific research
Ohio State Implementation

Active studies

- Accruing subjects
- Amend consent confidentiality section
- Use standard text
- Refer current subjects to NIH website for questions
Effective Oct 1, 2017, NIH will automatically issue CoCs to all research funded by NIH that is collecting or using identifiable, sensitive information. New disclosure rules apply to everyone. Learn more!

Certificates of Confidentiality (CoC)

CoCs protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations. NIH funded researchers are automatically issued a CoC through their award. Other Department of Health and
Notice Regarding NIH-Funded Studies

This notice applies to research funded by the National Institutes of Health (NIH) on or after December 13, 2016. Please review your copy of the study consent form to see if the NIH provided funding for the research.

The NIH updated its policy for issuing Certificates of Confidentiality for the research it funds. For more information, see NIH website. This Certificate protects private information about you (including your data and specimens) from legal proceedings. The information collected during your study cannot be disclosed unless you give your consent or a law requires that we disclose the information. If you were a participant in a study funded by NIH on or after December 13, 2016, contact your research team for more information about these protections for your data and specimens.
Ohio State Implementation

Active studies

- Study accrual complete
  - May update ICF, if other changes
  - Refer current subjects to NIH webpage for questions
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QUESTIONS?