Exemptions from IRB Review and the Revised Common Rule: What Has Changed and What Has Stayed the Same?

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Background & Terminology

- 45 CFR (Code of Federal Regulations) Part 46 refers to the DHHS regulations for the Protection of Human Subjects. It includes 5 subparts (A-E).
- Subpart A of 45 CFR 46 is the Basic HHS Policy for the Protection of Human Research Subjects.
  - It is also referred to as the “Common Rule”.
  - It was published in 1991.
  - Applies to all research involving human subjects that is conducted or supported by DHHS (e.g. NIH)
  - Fifteen other federal agencies have included Subpart A in their chapter of the Code of Federal Regulations and adhere to it for the research they conduct or support

Background & Terminology, cont.

- "The Common Rule" was recently revised with an effective date of June 19, 2018 and a **compliance date** of January 21, 2019.
  - It applies to all new human subjects research reviewed on and after January 21, 2019.
  - It is referred to as the "Revised Common Rule" (rCR), the "2018 requirements" and the "Final Rule".
  - Given these recent changes, the set of regulations that pre-date these changes are now referred to as the "Pre-2018 Requirements".

Background & Terminology, cont.

- **Research**: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(l))

- ***Human Subjects Research* (*"HSR"*):** Activities in which an investigator conducting research:
  - Obtains information or biospecimens through intervention or interaction with an individual **or** studies identifiable data or biospecimens.

  - This includes the use of coded data or biospecimens when the investigator has access to the code key.

Background & Terminology, cont.

- **FWA**: a Federalwide Assurance, an assurance of compliance that the institution will commit to follow the regulations for the protection of human subjects at 45 CFR 46.
  - When an institution is conducting DHHS-supported (e.g. from NIH) *human subjects research*, it is required to obtain an FWA through the *DHHS Office for Human Research Protections (OHRP)*.
    - FWAs are active for 5 years and must be renewed.

- All IRBs must also be registered with OHRP before they can review *human subjects research* under 45 CFR 46.

Background & Terminology, cont.

- Generally an institution conducts the IRB review of its own staff's *human subjects research* activities under a protocol (or provides a formal determination of exempt from IRB review).
  - With the introduction of the ***Reliance Agreement*** (also called ***Authorization Agreement***) and the "NIH Single IRB Policy", one institution's IRB may act as the IRB of record for another institution.
  - The reliance agreement is a formal contract which is executed between two or more institutions and outlines the HSR protection-related responsibilities of all parties for the lifetime of the protocol.
    - For example, NIH might rely on an external IRB who will review and have oversight for the *human subjects research* which is occurring at NIH (or vice versa).

Background & Terminology, cont.

- **"*Not Human Subjects Research*" (NHSR):** A research activity which does not involve human subjects nor meet the definition of *human subjects research*, e.g. studying de-identified data or biospecimens (with no access to a code key)
  - This concept is not addressed in the regulations.
  - This type of activity is not the same as exempt *human subjects research;* however, like exempt *human subjects research*, it does not require IRB review.

Background & Terminology, cont.

- ***Exempt Human Subjects Research*:** A research activity that meets the definition of *human subjects research* (i.e. involves interacting with human subjects or identifiable data or biospecimens); however, it is considered sufficiently low risk that it does not need meet the requirements for IRB approval and informed consent under the "Common Rule".
  - *Human subjects research* which is exempt from IRB review
  - In order for an activity to be considered exempt, it must meet specific criteria and the only involvement of human subjects must fall within one or more exempt categories as described in the "Common Rule".

Background & Terminology, cont.

- NIH does not execute reliance agreements to provide determinations of exemptions for other institutions' roles in *human subjects research*.
  - When exempt NIH research involves multiple institutions, these entities must obtain their own determination through an external IRB prior to the research beginning at those institutions.
    - This expectation is also true of entities which are subcontracted by NIH to conduct the research.
  - If the organization doesn't have an affiliated IRB, the NIH IC could provide funding so that the organization can seek external IRB review, e.g. by a commercial IRB.
  - If the other organization does not currently have an active FWA, it can apply for one here: https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/irb-registration/new-irb-registration/index.html

The rCR: Exempt Human Subjects Research

New Categories & New Criteria

- The pre-2018 Common Rule included six categories of exempt *human subjects research*.
- The revised Common Rule (rCR) contains some new exemption categories as well as some new criteria under the existing categories.
  - There are now eight categories of exempt *human subjects research.*
    - Only 6 of these are currently allowable for research being conducted by NIH staff given other NIH policies.
    - Only about 4 of these categories will likely be relevant to NIH research.

Exemption Category 1

- Applies to research in established or commonly accepted educational settings that involves certain normal educational practices, such as research on instructional techniques already in use or classroom management
  - This type of research is not regularly conducted at NIH; therefore, the provision of this determination has historically been infrequent here.

- New restriction for this category under the rCR:
  - The research must not be likely to adversely impact the student's opportunity to learn required educational content or the assessment of educators who provide the instruction.

Commentary provided by the Secretary's Advisory Committee on Human Research Protections (SACHRP) on this exemption category can be found here: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-b-november-13-2018/index.html.

Exemption Category 2

- Applies to research projects which involve data collection only through educational tests, surveys, interviews or observation of *public* behavior
- Most common exemption determination provided at the NIH
- Criteria which is the **same** as before:
  - (1) the data being collected as a part of the study and recorded cannot be readily linked back to the subjects, directly or through identifiers linked to the subjects; or
  - (2) any disclosure of the data would not place the subjects at risk of certain harms

Exemption Category 2, cont.

- Two notable changes as part of rCR:
  - The word “only” has been added to clarify that it applies to research that “**only** includes interactions” involving educational tests, surveys, interviews, and observation of public behavior, i.e. this category is not applicable to research involving interventions.

  - Sensitive, identifiable data may now be collected under this exemption, but an IRB member must conduct a **limited review** to determine that there are adequate privacy and confidentiality protections included in the study.
    - The protocol must include a section which explains how the investigator intends to protect the privacy and confidentiality of the subjects.

SACHRP has also provided some interpretive guidance relevant to this exemption category: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-b-november-13-2018/index.html

Exemption Category 2, cont.

- The restrictions from conducting research with children, under this category, have not changed.
  - Does not apply to survey or interview research with children
  - Does not apply to research involving public observation with children, when the researcher participates in the activities being observed

Exemption Category 3

- Applies to research involving only "**benign behavioral interventions"** (not applicable to biomedical interventions)
  - Brand new category under the rCR that may apply to NIH research

- A benign behavioral intervention must be:
  - Brief in duration (although data collection may take longer);
  - Harmless, painless, and not physically invasive; and
  - Not likely to have a significant adverse lasting impact on subjects or be offensive or embarrassing to subjects

Exemption Category 3, cont.

- Examples from OHRP:
  - Having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

- Other examples:
  - Laboratory sessions in which subjects complete a short task with a partner and complete measures of teamwork, personality, etc.
  - Auditory learning tasks in which subjects have to press the correct button or level in response to the sound
  - Sessions in which subjects read health communication messaging and their eye movements are tracked via video to see what text they focus on and for how long

Exemption Category 3, cont.

- Data collection must be limited to verbal or written responses, including data entry or audiovisual recordings.

- As with Exemption 2:
  - (1) the data being collected and recorded cannot be readily linked back to the subjects, directly or through identifiers linked to the subjects; **or**

  - (2) any disclosure of the data would not place the subjects at risk of certain harms; **or**

  - (3) sensitive, identifiable data may be collected as part of the project, but an IRB member must conduct a **limited review** to determine that there are adequate privacy and confidentiality protections included as part of the protocol.

Exemption Category 3, cont.

- Subjects must prospectively agree to the research.
- The investigator should take into consideration the subjects' population, the context of the research, the topic, and other characteristics of the study.
- This exemption is only applicable to research with adults (cannot be used for research with children).
- Waiting for more detailed guidance from OHRP on this new category

SACHRP commented on the types of activities that might meet this category and their interpretation of some of the requirements in a letter issued in July 2017: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-b-august-2-2017.html.

Exemption Category 4

- Exemption Category 4: Applies to secondary research of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
  - (1) when the identifiable materials are publicly available, or
  - (2) when the data is recorded by the investigator in a de-identified manner, i.e. no identifiers are accessible to the researcher once the analysis begins
    - For example, the researcher conducts a retrospective medical chart review and records the necessary data in a data sheet for future analysis without any personal identifiers nor a code which would allow the investigator to link back to subjects.

Exemption Category 4, cont.

- New provisions under the rCR:
  - Data and biospecimens no longer have to be in existence prior to the start of the research to qualify.
    - For example, a research study that proposes to analyze biospecimens or data that will be collected for clinical purposes in the future might qualify for this exemption.

Exemption Category 4, cont.

- This exemption category is seldom used at NIH because:
  - Most data at NIH is collected (or included) under the investigators' IRB approved protocols and is maintained in an identifiable format, i.e. very little data at NIH is considered clinical only.
  - The NIH IRP has BTRIS (The Biomedical Translational Research Information System) as a rich resource of de-identified clinical research data from IRB-approved protocols.
    - This data is available from 1976 to the present.
    - BTRIS allows investigators to have access to others' clinical and research data with no need to access identifiers at all, i.e. the BTRIS database or BTRIS staff act as an honest broker protecting the patients' identifiers from disclosure.

Exemption Category 4, cont.

- More new provisions under the rCR:
  - Secondary *human subjects research* that is conducted by or on behalf of a federal department or agency, using identifiable data collected or generated by the government for non-research purposes, e.g. QI/QA data
    - Data would have to meet federal privacy standards (e.g. be covered under the Privacy Act).
    - Data originally collected under NIH protocols, including clinical data, would not qualify.
  - The investigator must not plan to attempt to re-identify or contact the research subjects.

Exemption Categories 5 & 6

- Determinations of Exemption Categories 5 & 6 have been negligible at the NIH in the past
  - Exemption 5 applies to research involving public benefit or service programs.
  - Exemption 6 applies to research involving taste and food quality evaluation and consumer acceptance studies.

Exemption Categories 7 & 8

- These two categories are brand new under the rCR.

- They cannot be implemented at NIH at the present time.
  - Exemption 7 involves the storage or maintenance of identifiable data or biospecimens for secondary research.
  - Exemption 8 involves secondary research with identifiable data or biospecimens.

Exemption Categories 7 & 8, cont.

- Both exemptions require that the researcher has previously obtained "broad consent" for future research from the original research subjects.
  - “Broad consent” under the rCR involves a very specific and detailed set of elements that most current consent forms at NIH do not contain.
  - NIH has not yet decided to implement broad consent per the rCR.

What to Do If You Think Your Research Might Be Exempt…

- All NIH staff who wish to conduct exempt human subjects research must submit the project and receive a formal determination of an exemption before commencing any research activities.

- If unsure, the PI should contact julie.eiserman@nih.gov with a description of the project to learn if it might be a possible candidate for exemption from IRB review.
  - For more complicated projects, the PI should request an OHSRP consult.

NIH Policy Re: Submitting for an Exemption

Changes to the Submission Process

- As of January 21, 2019, all requests for exemptions must be submitted in iRIS, the electronic IRB submission system: https://irb.nih.gov/.

- All requests for exemptions will be reviewed by a designated staff member in the NIH IRBO.

Changes to the Submission Process, cont.

- Requests for exemptions now require submission of a protocol.
  - Much shorter in length compared to a protocol being submitted for IRB review and approval
  - Exempt protocol templates are available here: https://irbo.nih.gov/confluence/display/IRBO/Templates+and+Forms#TemplatesandForms-ExemptProtocolTemplateandGuidelines

Tips to Streamline the Exempt Submission and Review Process

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- When collaborating or contracting with other organizations to conduct *human subjects research** as part of the study, you should determine whether these organizations have a current Federalwide Assurance (FWA) and an IRB that can review the protocol and provide an exemption (or IRB approval) for their role in the project.

*These activities include screening for eligibility; communicating the elements of consent or reading the consent form aloud; asking questions via survey, interview or focus group (either in person, via phone or over the Internet); implementing the research intervention; and/or reviewing, analyzing or interpreting identifiable data for research purposes.

Tips, cont.

- Download and review the appropriate exempt protocol template for the type of research you are doing

- Use the template as a guide for writing your protocol, i.e. don't simply enter response text under the sections of the protocol template
  - The protocol should read like a narrative with headings and subheadings.
  - Delete any instructional language or questions found in the template
  - Be sure to review the template alongside your finished protocol before submitting to ensure that all of the required topics & sub-topics are addressed

Tips, cont.

- Be sure that your Branch Chief and all of the members of the research team at NIH have an active iRIS account, prior to submitting the project in iRIS.
  - Request accounts here: https://odprdoirapp.od.nih.gov/jira/servicedesk/customer/portal/3/create/20

- After completing the iRIS forms and uploading all of the required documents, be sure to route the project to your Branch Chief for approval.

Tips, cont.

- Request one-on-one training with the iRIS Training Team on submitting a request for an exemption and responding to requests for corrections/stipulations by emailing the iRIS training team at iris_training@od.nih.gov.

- Carefully read through and follow the instructions for submitting in iRIS
  - The process is not intuitive.
  - See Instruction Sheet 8 here: https://irbo.nih.gov/confluence/display/IRBO/NIH+iRIS#NIHiRIS-ResourcesforInvestigators,Navigators,andStudyTeams

Tips, cont.

- When completing the iRIS applications/forms, only answer that all study team members have met the training requirements *after* you have confirmed that they have.
  - Most exempt submissions require completion of the *CITI Social & Behavioral Educational Modules Basic Course.*
    - NIH researchers must have taken the most up-to-date version which became available on Jan. 21, 2019.
    - This course must be accessed through our web site under Required HRPP Training using an NIH log in and password: https://ohsr.od.nih.gov/nih/index.php
    - Eventually the link will move to the IRBO website: https://irbo.nih.gov/confluence/display/IRBO/Training+and+Education

Projects that Involve Prospectively Collecting Data from Humans

- Ensure that the protocol:
  - Includes a clear delineation of the roles of NIH and every other collaborating or contracting institution
    - In other words, who will conduct recruitment, screening, scheduling, consenting, data collection, transcription, access to identifiers linked to data, maintenance and cleaning of data, analysis, interpretation, manuscript writing, etc.
  - Defines the respective recruitment, screening and data collection plans and includes category specific screeners/instruments, when different categories of subjects are being recruited, e.g. patients, caregivers and health providers
  - Discusses use of panel-crowdsourcing companies for recruitment and screening and/or proprietary software tools for survey/task design, data collection or analysis, e.g. *Amazon Mechanical Turk* (Mturk), *Qualtrics*, *SurveyMonkey*, etc.

Projects that Involve Prospectively Collecting Data, cont.

- The approved written NIH informed consent template, which is used for IRB-approved research, is not required as part of exempt research, nor is documentation of consent (e.g. the subject's signature).
  - PI is expected to communicate some specific "elements of consent" to the subject:
    - The project is research
    - It's voluntary
    - The purpose
    - The time commitment and procedures/types of questions involved
    - Contact information for a study staff member who can answer questions
  - Possible modes of communication:
    - Verbal
    - Email
    - Paper handout
    - Introductory text in a paper or on-line survey instrument

Projects that Involve Prospectively Collecting Data, cont.

- Be sure that you create and submit all of the following as part of your exemption:
  - Recruitment materials
  - Screening questions
  - Consent language
  - Instruments (e.g. surveys, interview questions, focus group guides)
  - Any text or images that subjects will be required to review as part of the study
  - And mock ups of all tasks that you will ask subjects to conduct
  - Instructional language or scripts

Accessing this Presentation

- This presentation is being videocast and should be available for future viewing here: https://videocast.nih.gov/PastEvents.asp.

- To request a pdf of this presentation or ask questions about its content, please email me at julie.eiserman@nih.gov.

Questions