REGULATORY AND FUNDING CHANGES FOR HUMAN SUBJECTS RESEARCH

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So many acronyms....

- DHHS = Department of Health and Human Services
  - OHRP = Office of Human Research Protections
    - HSR = Human Subjects Research
- sIRB = Single IRB
- NIH = National Institute of Health
- FOA = Funding Opportunity Announcement
IRB Reviews

- Research vs. not research
- Human subject research vs. not human subjects research
- Exempt
- Expedited
- Full Board

- Renewals & modifications
- Noncompliance
- Unanticipated problems
- Complaints
## Changes to Regulations

<table>
<thead>
<tr>
<th>New Requirement</th>
<th>Impacts</th>
<th>Compliance Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Common Rule OHRP</td>
<td>Human subjects protocols</td>
<td>Protocols approved on or after January 19, 2018</td>
</tr>
<tr>
<td>sIRB NIH</td>
<td>Some NIH funded, multi-site human subjects research</td>
<td>Proposals submitted on or after January 25, 2018</td>
</tr>
<tr>
<td>Certificate of Confidentiality NIH</td>
<td>NIH funded HSR</td>
<td>Effective for NOA on or after October 1, 2017 Retroactive to December 13, 2016</td>
</tr>
<tr>
<td>Clinical Trials NIH</td>
<td>NIH funded human subjects research meeting revised definition of Clinical Trials</td>
<td>Proposals submitted on or after January 25, 2018</td>
</tr>
</tbody>
</table>
New Common Rule
New Common Rule: Applicability

- Protocols approved on or after January 19, 2018 must follow the new Common Rule

- Protocols approved prior to January 19, 2018 will continue under the current Common Rule
New Common Rule: Changes

- Change in definition of Human Subjects Research
- New exempt categories
- Elimination of Continuing Review for certain studies
- Changes to consent requirements/forms
- Changes to waiver of consent
- sIRB requirement in 2020 for HSR
Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
New Definitions

- “Identifiable private information” Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

- “Identifiable biospecimen” Identifiable biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with biospecimen.
Exemptions

- Currently there are 6, there will be 8
- **Limited review** introduced as a new concept for some exemptions
- Category 3 exemption – benign behavioral interventions
Current List of Exemptions

- Categories
  - 1 – Normal educational practice in a normal educational setting
  - 2 – Use of educational tests, survey procedures, interview procedures or observation of public behavior
  - 3 – Use of educational tests, survey procedures, interview procedures or observation of public behavior of elected or appointed public officials
  - 4 – Collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens
  - 5 – Research and demonstration projects which are conducted by or subject to the approval of department or agency heads on public benefit or service programs
  - 6 – Taste and food quality evaluation and consumer acceptance studies
New List of Exemptions

Categories
1 – Normal educational practice in a normal educational setting *
2 – Educational tests, survey, interviews, or observation of public behavior *
3 - Benign behavioral interventions with adults
4 - Secondary research uses of identifiable private information or identifiable biospecimens **
5 - Research and demonstration projects which are conducted by or subject to the approval of department or agency heads on public benefit or service programs
6 - Taste and food quality evaluation and consumer acceptance studies

* Minor changes
** Major changes
New List of Exemptions cont.

- 7 - **Storage or maintenance of identifiable private information or identifiable biospecimens** for potential secondary research. Broad consent is required.

- 8 - **Secondary research for which broad consent is required and was obtained.** This includes research involving the use of identifiable private information or identifiable biospecimens for secondary research use.
Introduction of “limited review”

- Under some of the new categories, exempt research would be required to undergo **limited IRB review** to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens.

- The **limited IRB review** requirements are designed to provide privacy safeguards to reduce the chances that the disclosure of identifiable private information will occur and lead to harm.
Exempt: Category 1 (45 CFR 46.104.d.1)

- **Research, conducted in established or commonly accepted educational settings**, that specifically involves 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. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
Exempt: Category 2 (45 CFR 46.104.d.2)

Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is de-identified

(ii) Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is identifiable and the IRB conducts a limited IRB review.

- **Subpart D (children):**
  - (i) & (ii) allowed for educational tests & observation of public behavior as long as researchers do not participate in the activities being observed.
  - **Not allowed for surveys; (iii) not allowed**
Exempt: Category 3 (45 CFR 46.104.d.3)

- This is a whole new category:
- (i) Research involving **benign behavioral interventions** in conjunction with the collection of information from an **adult** subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
  - (A) The information obtained is de-identified
  - (B) Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or
  - (C) The information obtained identifiable and the IRB conducts a **limited IRB review**
Exempt: Category 3 cont.

- (ii) **Benign behavioral interventions** are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include 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.

- (iii) If the research involves **deceiving** the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

- **Subpart D (children): Not allowed**
Exempt: Category 4 (45 CFR 46.104.d.4)

- Secondary research for which consent is not required:
  - Secondary research uses of **identifiable private information or identifiable biospecimens**, if at least one of the following criteria is met:
    - (i) The identifiable private information or identifiable biospecimens are publicly available;
    - (ii) Information, which may include information about biospecimens, is recorded by the investigator in a de-identified manner and the investigator does not contact the subjects, and the investigator will not re-identify subjects;
    - (iii) The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under the HIPAA regulations
Exempt: Category 5 (45 CFR 46.104.d.5)

- **Research and demonstration projects** that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

- Most likely not applicable to the research we do at CMU
Exempt: Category 6 (45 CFR 46.104.d.6)

- **Taste and food quality evaluation** and consumer acceptance studies:
  - (i) If wholesome foods without additives are consumed, or
  - (ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or an agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

- Most likely not applicable to the research we do at CMU
Exempt: Category 7 (45 CFR 46.104.d.7)

- **This is a whole new category**
- **Storage or maintenance for secondary research for which “broad consent” is required:** Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a **limited IRB review** and makes the determinations required by the broad consent regulations.

- This category would be used for repositories we used to review as expedited. **Data is collected under this exemption.**
Broad consent introduced

- Broad consent is used for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens obtained in accordance with the requirements informed consent;
- (ii) Broad consent is appropriately documented or waiver of documentation is appropriate.
- (iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
- Additional consent elements are required
Exempt: Category 8 (45 CFR 46.104.d.8)

- **This is a whole new category**
- Secondary research for which broad consent is required and was obtained. This includes research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
  - (i) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with informed consent regulations
  - (ii) Documentation of informed consent or waiver of documentation of consent was obtained
  - (iii) An IRB conducts a limited IRB review and makes the determination that the research to be conducted is within the scope of the broad consent
  - (iv) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results
- For these studies we would have previously handled them as expedited and confirmed with the consent that was previously approved for the original collection of data/specimens that secondary use was allowed/not prohibited. Now there's an actual category for them. Data was previously collected.
Expedited Review and Continuing Review

No changes to the expedited categories, yet

Change to requirement for continuing review

Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(i) Research eligible for expedited review
(ii) Research reviewed by the IRB in accordance with the limited IRB review
(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
   A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
   B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.
Check-In

- Exempt and expedited protocols will go through a “Check-In” process
- IRB is still required to oversee all human subjects research
- Exempt - 2 questions regarding status
- Expedited - a few questions regarding status
- Reminders will be sent every 2 years after approval to remind researchers to check in
- Can close study through the check-in process
Changes to informed Consent

- Broad consent
- Content changes
- Changes to waivers
Informed Consent new requirements:

(i) Informed consent must **begin** with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

(ii) Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that **does not merely provide lists of isolated facts**, but rather facilitates the prospective subject’s or legally authorized representative’s understanding of the reasons why one might participate.
Informed Consent new requirements:

Currently there are 8 required elements of informed consent. (These elements appear in the template consents found on our website.) A 9th requirement is added:

- **One** of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens **must** be included:
  - (i) A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens **could be used for future research** studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; **or**
  - (ii) A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used** or distributed for future research studies. (**not recommended**)

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**Note:** This document is for educational purposes only and should not be used as legal advice.
Waiver of Informed Consent New Requirements

Waiving informed consent means there is no consent form or consent process. Not commonly granted.

- Currently there are 4 criteria that need to be justified in order for the IRB to grant a waiver of informed consent. Now there will be 5.
- A new category is added:
  - If the research involves using identifiable private information or identifiable biospecimens, the research could not practically be carried out without using such information.
Waiver of Signed (Documentation of) Informed Consent

- These are granted commonly for telephone screens or online research
- No signed consent form
- A consent process is still followed:
  - A discussion with the potential participant
  - A document provided to the potential participant (online or in-person)
  - For in-person interactions a script is used to ensure all the elements of consent are covered
Waiver of Signed Informed Consent new requirements

An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

◦ (i) That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern;

◦ (ii) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or

◦ (iii) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
NIH Changes
NIH Funding @ CMU

- **Currently (September 2017) CMU has:**
  - Approximately 80 active NIH awards
  - Approximately 55 active NIH funded IRB protocols
  - Approximately 30 PIs with NIH funded protocols

- **A subset of future NIH funded HSR - IRB protocols will be impacted**
sIRB: Applicability

- NIH funded Human Subject Research wholly or partially supported by grants, cooperative agreements, contracts or NIH Intramural programs
- All competing grant applications (new, renewal, revision or resubmission) with receipt dates on or after January 25, 2018 and for contracts and solicitations issued on or after January 25, 2018
- Domestic sites
- Non-exempt protocols
- When same research protocol is being conducted at more than one site
- Excludes career development, research training or fellowship awards
sIRB: Requirements

- Requires that proposals for funding include a plan that includes a statement confirming that participating sites will adhere to the sIRB Policy and describes how communication between sites and sIRB will be handled
  - Designation of the sIRB
  - Execution of a Reliance Agreement between the sIRB and Participating Sites
  - Review by both sIRB and Participating Site IRB
sIRB: sIRB Responsibilities

Responsibilities may vary based on Reliance Agreement
- IRB of Record
- Conduct review of protocol in accordance with the regulations
- Approve protocol, consent forms, advertisements, etc.
- Review and address unanticipated problems
sIRB: Participating Site Responsibilities:

Responsibilities may vary based on Reliance Agreement

- Local context review (university specific requirements, local law, etc.)
- Review conflicts of interest
- Confirm training requirements are met
- Oversee conduct of research
- Report unanticipated problems to sIRB
Certificate of Confidentiality

- Effective October 1, 2017, retroactive to December 2016
- Rather than having to apply for a certificate of confidentiality, NIH will automatically issue one for NIH awards as part of the award terms and conditions
- Awardee institution and investigator responsible for determining applicability
- Consent forms will need to be modified (at time of renewal) to include new language about the certificate
Clinical Trials: applicability

- Only applies to NIH funded research that involves Human Subject Research and meets revised definition of Clinical Trials
Clinical Trial: New 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
Implications of being a clinical trial

1. Use appropriate Funding Opportunity Announcement
2. Complete Good Clinical Practices education
3. Write and follow a Data Safety Monitoring Plan
4. Register study with clinicaltrials.gov (within 21 days of enrolling first participant) and maintain the record throughout the study
Pre-Proposal:

- Notify OSP as soon as you know you’ll be submitting to NIH
Proposal: PHS Human Subjects and Clinical Trials

- Due dates on or after January 25, 2018
- Applicable to all NIH applications involving human subjects
- The NIH application form set removes the Human Subjects sub-section from the PHS 398 Research Plan
- NEW form for consolidated human subjects, inclusion enrollment report and clinical trial information
  - Data entry on the form
  - New attachments required: Recruitment and Retention Plan, Recruitment Status, Study Timeline
  - Additional data entry and attachments required for clinical trials
Proposals: FOAs

- **BRAIN Initiative: Development of Next Generation Human Brain Imaging Tools and Technologies (U01)** *(Clinical Trials Not Allowed)*
  (RFA-FB-17-004)
  National Institute of Biomedical Imaging and Bioengineering
  National Center for Complementary and Integrative Health
  National Eye Institute
  National Institute on Aging
  National Institute on Alcohol Abuse and Alcoholism
  Eunice Kennedy Shriver National Institute of Child Health and Human Development
  National Institute on Drug Abuse
  National Institute on Deafness and Other Communication Disorders
  National Institute of Mental Health
  National Institute of Neurological Disorders and Stroke
  Application Receipt Date(s): December 20, 2017 and December 11, 2018, by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on these dates. No late applications will be accepted for this Funding Opportunity Announcement. Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

- **Women's HIV/AIDS Cohort Study (WHCS ) (R01)**
  (RFA-HD-18-010)
  Eunice Kennedy Shriver National Institute of Child Health and Human Development
  National Institute of Dental and Craniofacial Research
  Application Receipt Date(s): December 15, 2017, by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on this date.

- **Limited Competition: Small Grant Program for NHLBI K01/K08/K23 Recipients (R03)** *(Clinical Trial Optional)*
  (RFA-HL-18-025)
  National Heart, Lung, and Blood Institute
  Application Receipt Date(s): February 15, 2018; June 15, 2018, by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on these dates. No late applications will be accepted for this Funding Opportunity Announcement. Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.
Proposal: PHS Human Subjects and Clinical Trials Information

- NIH Resources Available
  - NIH Annotated Form Set
  - NIH Video of New Form
Changes to SPARCS

- Common Rule
  - Upload your protocol (eligibility pages for exempt)
  - Check-In
  - sIRB
    - Added questions
    - Upload reliance agreements
- Clinical Trials
  - Added a question
- Proposals
  - SPARCS proposals went live 10/30/2017
SPARCS User Experience

- Small changes to reviewer and researcher experience
  - Upload protocol means fewer reviewer notes

- Freeze period

- “Turn on” new version of SPARCS IRB early January 2018
Transitions for SPARCS

To accommodate the transition to the new regulations, the following is planned for protocol submission via SPARCS:

**Between December 20, 2017 and January 3, 2018 no new IRB protocols can be submitted.**

- During this time, protocol modifications and continuing reviews will be accepted and will be handled under the “pre-2018” HSR regulations. This limited interruption of service is necessary to implement the new regulations.
- Protocols approved prior to January 19, 2018 will continue to be governed by the “pre-2018” HSR regulations for an undetermined period of time.

**Beginning on January 4, 2018 new IRB protocols may again be submitted via SPARCS**

- Any new protocols submitted on or after this date will be subject to the new HSR regulations and can be approved on or after January 19, 2018.

The IRB office will be especially busy during December and January so we’d really appreciate it if protocols are submitted well in advance of the anticipated start date.

*If a funding agency requires that a study be submitted and approved during this time period, the IRB will work with the researcher to accommodate the request.*
Information & Assistance

◦ IRB Website:
  http://www.cmu.edu/research-compliance/human-subject-research

◦ IRB Mailbox:
  irb-review@andrew.cmu.edu

◦ Contacts:
  ◦ Teri Reiche        treiche@andrew.cmu.edu
  ◦ Doug McFarland    dougmc@andrew.cmu.edu
  ◦ Jill Schaefer      jsschaef@andrew.cmu.edu
  ◦ Susan Brunner      sebrunne@andrew.cmu.edu
  ◦ Gail Kusbit        gkusbit@andrew.cmu.edu
Questions?