Brief Introduction to Review of Human Subjects Research

Introduction to Research Course
Department of Medicine

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Regulations & Policies
What regulations can apply?

- Common Rule – most federally funded research
  - Dept of Health and Human Services version is 45 CFR 46
- Food & Drug Administration (FDA)
- Veterans Administration
- Health Insurance Portability & Privacy Act (HIPAA) Privacy Rule
- Family Educational Rights & Privacy Act (FERPA)
What other policies/requirements apply?

- **UW-Madison**
  - Human research protection program (HRPP) policies
  - Specific IRBs’ guidance
  - Conflict of Interest policy

- **State**

- Policies or requirements that are specific to other entities involved in the research, such as:
  - Granting agencies
  - School districts
  - Other

- For HRPP policies, see: [http://www.grad.wisc.edu/research/hrpp/HRPPpolicy.html](http://www.grad.wisc.edu/research/hrpp/HRPPpolicy.html)

- For HS IRBs guidance, see: [https://kb.wisc.edu/hsirbs/18837](https://kb.wisc.edu/hsirbs/18837)
Definition of Human Subjects Research
Federal Definitions – Common Rule

- Research is defined by the Common Rule as, “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”

- A human subject is defined under the Common Rule as “a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.”
FDA has defined "clinical investigation" to be synonymous with "research". "Clinical investigation" means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

Human subject is defined by the FDA as “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.”
Examples of human subjects research

Covers a wide variety of activities, including studies of:

- Human testing of drugs, devices, or products developed through research
- Data from surveys, interviews, and observation
- Employment information or records of earnings
- Medical records
- Bodily materials, such as cells, blood, urine, tissues, organs, hair, nail clippings, or DNA, when these are linked to specific individuals
Exempt Research

- IRBs, not researchers, make the determination as to whether a research protocol is exempt
- Common examples of exempt research
  - Questionnaires, surveys, interviews that are anonymous or not sensitive
  - Chart review studies and no identifiers are recorded
  - Evaluations of educational techniques, curricula when the intent is to publish
Not Human Subjects Research

- IRB Office reviews to determine whether it meets the federal definition of “research” and/or of “human subject”
  - Once determination made no further interaction with IRB for project needed unless project begins to meet definition of research and/or includes human subjects

- Examples of not research
  - Program evaluation, quality assurance activities

- Examples of not involving human subjects
  - Use of coded data when researchers do not have access to the key to the code and entity holding code will not release link to researchers
  - Research on decedents
Difficult to determine sometimes whether a project constitutes research rather than QI/QA or program evaluation

May be research if:
- There is an intent to publish
- Procedures involve randomization
- Standard of care is altered
Case Studies/Case Reports

- Case reports involving three (3) or fewer patients generally do not require review by a UW-Madison IRB because they are not viewed as meeting the definition of research under the Common Rule.
- HIPAA Privacy Rule may apply.
Engagement in Human Subjects Research

- The UW-Madison follows guidance set forth by the Office for Human Research Protections (OHRP) regarding when an individual may be considered engaged in human subjects research and thus needs IRB oversight.

- Examples of engagement in human subjects research:
  - Holding the federal grant that supports research involving human subjects.
  - Intervening for a research purpose with humans.
  - Obtaining informed consent.
  - Obtaining private information about people or using identifiable biological specimens.
What to do If IRB Review Is Required
See the New Investigators Guide at:

https://kb.wisc.edu/hsirbs/23426
Determine which IRB has the purview to review the project

- There are two health sciences IRBs (Health Sciences IRB & Minimal Risk IRB), the Social & Behavioral Sciences IRB, and Education IRB.

- The Health Sciences IRBs have contracted with a commercial IRB, Western IRB, to review most of the industry-sponsored clinical research.
If the research involves sites/personnel not under UW-Madison purview

- May need to work with more than 1 IRB
  - IRB oversight may be required for each site
  - There are cases when one IRB will defer oversight to another
    - Wisconsin IRB Consortium (WIC): Aurora, Marshfield, Medical College of WI, and UW-Madison HS IRBs have an agreement for deferral to one another

- Sites that do not have IRB
  - Personnel engaged in human subjects research may need IRB coverage
Determine who can serve as PI

- UW-Madison policy allows the following to serve as PIs on a project involving human subjects research
  - Individuals with a UW-Madison faculty appointment (generally, a 50% or more appointment). This includes faculty with a full-time UW-Madison position but who hold a $0 UW-Madison appointment only because their position is funded by the federal government.
  - Individuals with a UW-Madison Clinical/Health Sciences (CHS) appointment.
  - UW-Madison unclassified staff (academic staff and limited appointees) who have obtained approval of their Chair/Director using the form “Request for Approval to Serve as Principal Investigator on a Human Subjects Protocol”. (This includes Emeritus professors).
  - UW-Madison postdoctoral scholars, visiting faculty, or visiting academic staff who have obtained approval of their Chair/Director using the form “Request for Approval to Serve as Principal Investigator on a Human Subjects Protocol”
  - UWHC employees with the approval of their supervising UWHC Vice President
  - Individuals who have an appointment at the William S. Middleton VA Hospital with approval of the VA Research & Development Committee

- NOTE: Students generally cannot serve as PIs
Complete required training

- Human subjects protection training (UW-Madison CITI modules) required for all UW-Madison faculty, staff, and students engaged in human subjects research unless VA human subjects protection training completed instead

- If within the Health Care Component, HIPAA Privacy Rule training for researchers also required

- Any training relevant to the conduct of the proposed research
Identify whether there is a potential financial conflict of interest

- Campus policy restricts participation in human subjects research when individuals have a significant financial interest in the entity or entities that a) sponsors the study, or b) owns or licenses a technology tested in the study when the interest meets or exceeds one of the following thresholds:
  - Compensation of $20,000 or more in a calendar year from a business entity
  - An ownership interest in a publicly traded business entity valued at $20,000 or more or a 5% or greater equity interest
  - An ownership interest in a privately held business entity
  - A leadership position in a business entity (Leadership positions are positions with fiduciary responsibility, including senior managers (e.g. presidents, vice presidents, etc.) and members of boards of directors. Scientific advisory board membership is not a leadership position)

- Potential financial conflicts of interest must be disclosed to the reviewing IRB under campus policy
Become familiar with how to submit a project to the IRB

- All campus IRBs now require electronic submission of applications
- Health Sciences IRBs use ARROW
  - Training materials and FAQs are available on the HS IRBs website at [www.medicine.wisc.edu/irb](http://www.medicine.wisc.edu/irb)
- Other campus IRBs use Webkit (will use ARROW in future)
Become familiar with what an IRB assesses when reviewing applications

- Whether the study is as safe as possible for people to take part in the study
- If there are serious risks
  - they are as low as possible
  - the right kind of monitoring is in place to prevent adverse effects or identify adverse outcomes as soon as possible
- Whether the subject population is the appropriate population to answer the study question
- Whether the study design is acceptable so that
  - the question posed can be answered by the research
  - the right number of people will be enrolled (not too many or too few) so that as few people are exposed to risk as possible
- Whether the information given to potential research participants is sufficient to allow an informed choice about taking part in a research study
- Whether privacy and confidentiality are adequately protected
- Whether recruitment strategies are appropriate
- Whether regulatory and institutional requirements are met
IRB Review Process: Health Sciences IRBs
Health Sciences IRBs Submission Process
May 28, 2009

Submission of New Protocol by Research Team

- Communication with Research Team
  - Cancer Center Scientific Review
    - To the IRB for triage
      - OR
        - No institutional scientific review needed
          - OR
            - Institute of Clinical & Translational Research (ICTR) Scientific Review
              - Communication with Research Team

- Communication with Research Team
  - Pre-Review by IRB Staff
    - IRB Review
      - Modifications requested
        - Communication with Research Team
          - APPROVAL

- APPROVAL
Overview of Submission and Review Process for Full Board Review (I)

- Electronic copy of application sent to the IRB Office first
- IRB Office will send to scientific review committee if needed
- If no scientific review required, the application will be forwarded to an IRB reviewer
- If scientific review required, IRB review does not proceed until the scientific review committee agrees the study can be forwarded to the IRB for review
Overview of Submission and Review Process for Full Board Review (II)

- If no scientific review needed or the scientific review committee approves, a staff reviewer will work with the study team to address any missing information, revisions needed to ensure the study complies with campus and federal policies and IRB review conventions.
- 2 cycles of feedback are given by the staff reviewer.
- Once the pre-review is complete, paper copies are then requested and the study is scheduled for review by the full IRB.
Pre-Review Concentrates On…

- Completeness, accuracy of application
- Compliance with
  - institutional policy (e.g., PI qualifications, training requirements, COI issues)
  - State Law
  - federal regulations
    - Common Rule
    - FDA regulations, if applicable
    - VA regulations, if applicable
  - other institutional precedents
- Spotting major issues that will be a challenge at the formal review stage
IRB Review of Grants

- Federal regulations require IRBs to review federal grants to ensure they are concordant with the IRB-approved protocol.
- If the grant does not match the IRB protocol, a new IRB application may be needed or a change of protocol to bring the application in line with the grant.
- Grants cannot be added to a study until they are awarded.
- When the IRB has approved the addition of a funding source, it appears in PLUS.
Grant Titles

- The title of the IRB application and the grant are not required to match, but many funding agencies and RSP prefer them to match
  - Matching titles cannot be done when several grants support one IRB application
Just-in-Time/Approval of Protocol Concept

- If a PI has been informed that his or her grant is likely to be funded or human subjects activities do not occur until after the first year of the grant, the PI can submit a Protocol Development Activities Only Application (aka PDA) to the IRB.

- PDA allows for approval of the grant concept and for funds to be released while the PI works on a “full” application.

- Occasionally funding agencies will not release funds until “full” IRB approval is granted.
After Initial IRB Approval
Post-Approval Requirements

- Exemption granted/Not human subjects research determination: do not need to communicate with IRB further unless project changes in a way that suggests the exemption status has changed
  - Encouraged to close exemptions with the IRB when completed

- Non-exempt research (full or expedited initial review)
  - Continuing review progress report required at least annually – must be provided to the IRB with sufficient lead time in order to avoid an expiration
  - Changes of protocols are expected to be approved by the IRB before they are implemented (unless to avoid an apparent immediate hazard to subjects)
  - Noncompliance, potential unanticipated problems, and new information must be reported to the IRB in a timely manner
  - Closure report should be submitted to the IRB when study activities involving human subjects are complete
How to Contact the IRBs
Health Sciences IRBs

- Suite 105, 800 University Bay Drive
- View the WEBSITE at www.medicine.wisc.edu/irb - contains policies, guidance, forms, news/updates
- CALL the HS-IRBs Office at 263-2362 - we have nice, smart staff on call daily who can help you
- EMAIL us at AsktheIRB@medicine.wisc.edu – general questions answered promptly
- Make an APPOINTMENT for a consultation
- Questions about ARROW – email askarrowirb@medicine.wisc.edu or call 262-0041
- Join our LIST-SERV – sign up to receive regular updates and newsletters from the IRB
Education & Social & Behavioral Sciences IRBs

- Website: http://www.ls.wisc.edu/ors/IRB/IRB_Home.html
Questions?