



Understanding the IRB Review Process and Responding to IRB Notices

Health Sciences and Minimal Risk IRBs

Workshop Overview

- Introductions
- What Happens to IRB Applications
 - IRB Review Criteria
 - Common Application Problems
- Responding to Modification or Deferral Notices
 - Questions?

Submissions with IRB Deadlines or Reporting Timeframes

- Initial Review applications
- Changes of protocol (non-expedited)
- Continuing Review Progress Reports
- Reports of serious adverse events, unanticipated problems, or noncompliance

Submissions without IRB Deadlines

- Exemption applications
- Expedited changes
- Modification responses
- Deferral responses



What Happens to New Initial Review Applications

IRB Office Processing

- Processed into database and placed on next meeting agenda (agendas not capped)
- Often reviewed by IRB Office Director and, if incomplete or likely to be deferred, held and comments provided to the point of contact via email
- Assigned to staff reviewer and IRB members
- Staff reviewers prepare detailed analyses for IRB members
- Staff reviewers mediate between researchers and the IRB to help facilitate review and approval process

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What Happens to New Initial Review Applications

The Review Process

Produced by University Communications

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IRB Review Criteria: Regulations

- Common Rule (45 CFR 46)
 - Basis for IRB authority and review
 - Outlines criteria IRBs use to approve a study
- FDA Regulations
 - Cover experimental drugs and devices
 - Do not allow for waiver of consent
- VA Regulations
- HIPAA Privacy Rule

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IRB Review Criteria: Risks to Subjects are Minimized

- IRB focuses on this criterion especially
- IRB reviews study and statistical design
 - If risks low, study design less scrutinized
 - Risky procedures require justification
 - As few subjects as possible should be exposed to risk to answer research question

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Assessing Minimization of Risk

- Are subjects being deprived of standard of care?
- Are subjects being removed from medications (e.g. placebo) or undergoing a sham procedure?
- Are research procedures piggybacked on clinical procedures?
- Are type of data being collected appropriate for the research question?

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IRB Review Criteria: Risks Reasonable in Relation to Benefit

- If any risk to subjects, benefits must outweigh risks of study participation
- Risks may be direct (e.g., adverse effect from study drug) or indirect (e.g., withdrawal from currently effective treatment)
- Benefits may be direct (e.g., subject is helped) or societal (e.g., knowledge derived from study may lead to new treatments)

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Assessing Risk/Benefit Ratio

- If any risk to subject, is there a direct or societal benefit?
- Higher the risk, greater expectation for direct benefit to subjects
- Do eligibility criteria minimize risks?
- Are study procedures justified, especially risky ones?
- Is monitoring of subjects and study adequate?



IRB Review Criteria: Selection of Subjects is Equitable

- IRB takes into account purposes of the research and its setting
- IRB pays particular attention to enrollment of vulnerable populations (e.g., children, prisoners, mentally disabled persons, or economically or educationally disadvantaged persons)



Assessing Subject Selection

- Is the target population appropriate to answer the research question?
- Are any individuals being excluded or targeted for inclusion without justification?
- Will the subject population benefit from the outcome of the research?



IRB Review Criteria: Informed Consent Process

- Common Rule & FDA regulations assume that written informed consent will be obtained – justification needs to be provided if not doing so
- Investigator must propose a consent process (not just a form) that is appropriate for the subject population



Assessing the Informed Consent Process

- Is an informed consent process provided?
- Is the consent process appropriate for the subject population – special consent process required for subjects with impaired decision-making or who are illiterate, blind, or have limited English-speaking abilities
- Does the consent document contain the required elements of consent and is the reading level (8th grade or lower) appropriate?



IRB Review Criteria: Data and Safety Monitoring

- For more than minimal risk studies, IRB requires a data and safety monitoring plan
- Plans may include a Data Safety and Monitoring Board (DSMB) or Data Monitoring Committee (DMC)
- IRB typically requires more than minimal risk investigator-initiated studies to have a DSMB or DMC



Assessing Data and Safety Monitoring

- How will individual subjects be monitored?
- Is the monitoring appropriate for the risk level (e.g., frequency of visits, types of laboratory tests)?
- Is data being monitored such that trends can be detected and the study changed should a problem arise?



IRB Review Criteria: Protecting Subject Privacy and Confidentiality

- The greater the potential for harm a breach of confidentiality may pose to subjects, the greater the need for robust measures to protect subject data
- Generally, IRB expects data to be secured in a manner commensurate with medical records



Assessing Privacy and Confidentiality Protections

- Where will data be stored (e.g., secure password-protected computer v. flash drive)?
- Who will have access to study data?
- Will the data be coded and where will the code be kept?
- Will data be de-identified at the earliest opportunity?



IRB Review Criteria: Administrative Issues

- Applications are expected to be complete – missing information raises questions
- IRB will defer poorly prepared applications even if the research is likely low risk
- Well-prepared applications receive fewer modification requests, hence the review process goes faster



Assessing Administrative Issues

- Is the application complete?
- Does the information provided in the abstract, study description, and protocol match?
- Are questionnaire answers consistent with the study as described?
- Are all supporting documents provided (e.g., recruiting materials, surveys) and are they consistent with the application?



Common Application Problems

- Clear rationale and endpoints not established
- Does not describe standard of care nationally and at UWHC and how protocol alters patient care
- Eligibility criteria overly broad or vague
- Does not adequately identify risks or describe how they will be minimized
- Consent process not described in detail
- No additional safeguards for vulnerable populations



Receiving Modification Notices

- Expect to receive a modification notice
- Modification notices request additional information needed by the IRB in order to approve a study – they are not critiques of studies or investigators
- Modification notices are carefully prepared to convey the IRB's concerns as clearly – and politely – as possible



Responding to a Modification Notice

- Prepare a cover letter that responds point-by-point to the IRB's requests and is signed by the PI
- Response should use the same numbering as the modification notice
- Including text of IRB request in the response is helpful



Responding to a Modification Notice

- Be as specific as possible in the cover letter – do not just refer to the application or protocol
- Do not just state "Done" or "Change made"
- Be sure to respond to all of the IRB's requests – missing information will further delay the approval



Responding to a Modification Notice

- If a PI disagrees with an IRB request, response should include a rationale for why the PI believes the request was in error or provide additional information as to why the request should be rescinded
- If a request is unclear or you have questions about how to respond, contact the IRB staff person listed on the modification notice for assistance



Submitting Documents with a Modification Response

- If changes to protocol or IRB application were required, revise these documents, highlight any changes, and provide a copy of the revised documents with updated version and date
- If consent/assent forms were changed, provide two copies of each: one with highlighted changes and one unmarked copy with updated version number and date



Submitting a Modification Response

- Cover letter must be signed by the PI
 - Be sure to include the following: "I have read the above and take full responsibility for it."
- Cover letter also should include the protocol number and state that it is a response to a modification notice



Responding to Deferral Notices

- When IRB defers a protocol, either substantive concerns have been raised about the submission or the submission was determined to be incomplete
- No deadline to respond, but IRB Office determines when it can be scheduled for review, which depends on the IRB's workload



Responding to Deferral Notices

- Requires resubmission of the entire Initial Review Application and supporting materials, plus a cover letter that responds point by point to IRB requests or concerns
- Call staff reviewer for assistance in responding and determining when the response can be scheduled for IRB review



If you choose not to respond to an IRB notice

- Please submit a Closure Report form, otherwise the IRB Office will terminate your protocol 6 months after the last IRB review if no response received
- Failure to submit a Continuing Review Progress Report or modification requests related to progress reports can result in suspension of the protocol



IRB Updates

- New and improved website – new guidance, new forms, more resources
- AAHRPP accreditation site visit will be September 24-27
- More workshops on the way!



Questions?