Working with the IRB

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Overview

• Purpose
• Review Procedures
• Approval Criteria
• IRB Reviews
• Responsibilities of the Institution
• Revised Federal Rule
• Pearls & Pitfalls
• Recommendations
Purpose

• An “appropriately constituted group” designated to review and monitor 1) research involving human participants, 2) emergency use or expanded access (compassionate use) treatment, and 3) Humanitarian Use Device (HUD).

• IRB review assures appropriate steps are taken to protect the rights and welfare of research subjects and participants in expanded access and HUD treatment.

• When designated, can also act as a “Privacy Board” to review use of Protected Health Information (PHI) in research.
Question 1
In addition to reviewing research involving human participants, the Institutional Review Board (IRB) is also responsible for approving which activity?

1. Publications that result from the research
2. Clinical Trial billing of insurance or Medicare
3. Reliance agreement to defer to another IRB
4. Emergency Use or Expanded Access Treatment
Regulatory Definition
“Research Involving Human Subjects”

• Non-regulated research – does not meet the definition of research and human subject in Common Rule (45CFR46) and FDA (21CFR50 & 56)

• Exempt human subject research – meets the definition of research involving human subjects and only involves one or more “exemption” categories.

• Non-Exempt human subject research - meets the definition of research involving human subjects and is not eligible for “exemption”
Review Procedures – Non-Exempt HSR

• Expedited Review – certain kinds of research involving no more than minimal risk, and for minor changes to approved research
  • May be carried out by Chair or a member designed by the Chair
  • Reviewer exercises all authorities except may not disapprove

• Non-Expedited Review (Convened Meeting or Full Board)
  • Quorum requirements, voting rules, IRB policies & procedures

Question 2
Expedited review procedures can be used to approve certain kinds of research involving no more than minimal risk research and for what other activity?

1. Minor changes to approved research
2. Addition of an investigational drug
3. A progress report for a more than minimal risk study with subjects on active treatment
4. A new study involving an investigational device
Criteria for Approval

- **Risks** to subjects are minimized:
  - by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and
  - whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes

- **Risks** to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

- **Selection** of subjects is equitable.

- **Informed consent** will be sought from each prospective subject or the subject's legally authorized representative (LAR)*

Criteria for Approval (continued)

- **Informed consent** will be appropriately documented or appropriately waived*

- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

- When appropriate, 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.
Review by IRB

• Initial Review of new studies
• Continuing Review - Progress Report (greater minimal risk, some minimal risk where IRB determines review provides greater protection)
• Modification/Amendment
• Prompt Report of Unanticipated Problems Involving Risks to Subject or Others
• Prompt Report of Serious or Continuing Noncompliance
Relying Institution Responsibilities

• Human Research Protection Program (and policies)
• Implementation of HIPAA
• Education & Training of research personnel
• Research credentialing, if applicable
• Identification and analysis of Conflict of Interest
• Compliance or Quality Assessment programs
• Contracts or Clinical Trial Agreements
• Data Ownership, Export Controls, Record Retention
• Medicare Coverage Analysis & Billing Risk
Original Rule (Pre-2018) vs. Revised Rule (2018)

• Most of the exemptions under the “Original Rule” are still applicable under the “Revised Rule”.
• New exemption options – all require the new “Limited IRB Review” procedure.
• Eliminated certain continuing reviews (most minimal risk research).
• Eliminated “congruency” review of grant applications.
• Use of Single IRB review.
• Informed consent must begin with “key information” to facilitate comprehension.

https://www.youtube.com/watch?v=APRVsvKsPrM&feature=youtu.be
Requirement for Single IRB Review

- Compliance Date: January 20, 2020 (NIH policy Jan 2018).
- Applicable: US Institutions engaged in cooperative federally funded research for the portion conducted in the US.
- Not Applicable: more than single IRB review required by law.
- Not applicable: any Federal department or agency determines and documents use not appropriate for the particular context.
**Question 3**
Compliance with the Revised Common Rule (except for Single IRB review) starts

1. September 2015
2. June 2018
3. January 2019
4. January 2020
Reliance Agreement

• Relying Institution and organization operating the IRB document the reliance and responsibilities of each entity.
• Flexibility in how the agreement is documented.

SMARTIRB

• A platform designed to support single IRB review
• Tracks reviewing IRBs and relying institutions
• Harmonization guides
Key Information – Informed Decision

• Must be provided first.
• Information about why one might or might not want to participate
• Often includes information about:
  • Voluntary participation.
  • Purpose
  • Risks
  • Benefits,
  • Alternatives
• Must be presented in concise and focused manner

https://www.youtube.com/watch?v=F6PBlvN8RKA&feature=youtu.be
Question 4
Key information for informed consent often includes which element?

1. How to contact the Principal Investigator.
2. Whether the participant will be paid.
3. List of entities what will receive private health information
4. Risks
Minimal or No Change

• Greater than minimal risk research
• FDA regulated research (drugs, biologics or devices)
• Research involving Children
• Research involving Prisoners
• IRB approval of modifications prior to implementation
• Prompt reporting of UPIRSOs and serious or continuing NC

https://www.youtube.com/watch?v=zDsUUs9j3sQ&feature=youtu.be
Question 5
The Revised Common Rule significantly changed which section of the original rule?

1. FDA regulated research
2. Amendments to approved research
3. Research involving Children
4. Exemption categories
“Transitioning a study”

• Each institution can make the voluntary decision to switch a study approved under the “original rule” to comply with the “revised rule”
• Potential for confusion regarding which rule to follow for a specific study

Investigator Pearls & Pitfalls
Sources of Problems

- Ineffective communication with study staff
- Inadequate supervision or oversight
- IRB application becomes disconnected from actual study procedures
  - Changes to study procedures are made without IRB approval
  - Study team don’t have access to current version of IRB application
  - Lack of study team training when study is revised
- Current approved version of consent form(s) not managed
  - Associate Investigators or coordinators don’t have access to current version
Recommendations

• Use the IRB Administrator as a Resource prior to submission
• Complete the required training before starting the process
• Design the study with the regulations in mind
  • Definitions, waivers, exemptions
• Remember, procedures that are required by the study plan are “research procedures” regardless of whether they are “routine care”
• Include flexibility in the methods, wherever possible
• Avoid inconsistencies in the application, consent, and other documents
• Grant application is similar but not the same as IRB Application
Recommendations

• A schema or diagram of the study schedule is especially helpful for multi-arm studies

• Always include a “Schedule of Activities” or activity grid (table with procedures in rows and visits in columns)

• Be knowledgeable about other institutional issues and committees
  • Safety Committees (Radiation, Biologic, Chemical)
  • Approval at other study sites (e.g., affiliate hospital)
  • Support from service providers (e.g., laboratory, radiology)
  • Sponsored Programs (e.g., grants and contracts)
  • ClinicalTrials.Gov registration
  • IND, IDE or HDE from FDA
Questions