

# How to Review a New IRB Protocol

Per federal regulations, 45 CFR Part 46.111 (DHHS) and 21 CFR Part 56.111 (FDA), in order to approve research the IRB must determine that all of the following requirements are satisfied:

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

2. **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.**

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).

The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. **Selection of subjects is equitable.** In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
4. **Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45CFR Part 46.116 (General requirements for informed consent).**
5. **Informed consent will be appropriately documented or appropriately waived in accordance with 45 CFR Part 46.117 (Documentation of informed consent).**
6. **When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.**
7. **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 will be included in the study to protect the rights and welfare of these subjects.

## Committee Meeting Reviews in ePIRATE:

1. **Read the assigned materials at least 2-3 days in advance of the meeting.** ECU utilizes a primary reviewer system; therefore, if you are assigned as either the primary or secondary reviewer it is your responsibility to thoroughly review the IRB application materials and compare the information in the application with whatever other materials are provided (e.g., investigator's brochure, grant proposal, protocol, etc.) in advance of the meeting. All members are expected to review, at minimum, the IRB application (Smart Form) and consent document.
2. **Getting questions answered before the meeting.** IRB Members are not expected to be the absolute experts about the protocols they are assigned to review. Talk with others as needed. Feel free to contact the:
  - IRB Chair
  - Co- reviewer
  - Informal Consultant\* (e.g., colleague w/ expertise)
  - UMCIRB staff

Furthermore, do not hesitate to contact the Lead Researcher if you have questions and feel comfortable initiating this communication. Collegial interaction between researchers and IRB members facilitates the IRB review process and research compliance as well as fosters respect for human subject protections.

All contact with the research staff in ePIRATE may be done via a Public Comment activity, but keep in mind that if the request for information is lengthy it will take up a significant amount of space in the workspace). Conversations with the research team by phone may be documented in the IRB members review. Email correspondence may also be documented in the IRB members review, uploaded as an attachment to the review or copied and pasted in to the review.

Note: Once the submission has been assigned to the committee, the research team WILL NOT be able to edit their submission prior to the meeting.

3. **Contact the IRB Chair and UMCIRB staff if you have serious concerns about the protocol.**

Serious concerns would include such things as determinations that the risks outweigh any potential for benefit, either to the participant or society; that the procedures are novel and no supporting documentation regarding animal studies or background information has been provided; or that the proposed research procedures cannot provide answers to the research question or objective.
4. **Submit Your Review Prior to the Meeting** and be prepared to discuss and present your concerns to the Committee. You will do this by clicking the Submit Primary (or Secondary) Review activity button on the left-hand side of the workspace. The reviewer checklist form will guide you in providing the information necessary for the IRB meeting and you will be asked to choose one of the following recommendations:
  - **Approved**
  - **Approved with modifications**

- **Deferred (pending changes)**
- **Approval Denied**
- **Not reviewed**

You will also be asked to recommend a risk level and period of approval.

Study descriptions will be available in the SmartForm for each study to be reviewed by all committee members. Further study information can be found in the protocol and consent document(s) that are attached in the SmartForm. Member reviews should include controverted issues that require discussion and should list modifications/clarifications that are required to meet the criteria for IRB approval.

\* Informal verbal consultation is encouraged. However, IRB members must uphold the confidentiality agreement by maintaining all committee proceedings and documents that contain personal, confidential and proprietary information in strict confidence.

## **The process of reviewing a new IRB protocol:**

1. **Read the consent document first.** The consent document should be in lay language and therefore, should provide a good introduction to the research.
  - First read the consent form for general information about the study;
    - i. Can you clearly describe the study after reading the Consent Form?
    - ii. For studies involving medical treatments, can you distinguish standard-of-care from research procedures?
  - Then read it again for readability (6th—8th grade level);
    - i. Did it seem easy, or did you have to re-read it for understanding?
    - ii. Can a junior-high school student explain the study after reading the consent form?
2. **Read through the Smart Form and protocol description.** Although the language may differ; the narrative and the consent form should be consistent in the description of the purpose of the study, the procedures, the study timeframe, the possible risks and potential benefits, compensation and costs, confidentiality of data, etc. Consider the following questions:
  - **Background and Purpose of the Study**
    - i. Are the specific aims, hypotheses, and research questions clearly identified?
    - ii. Is there sufficient preliminary data to justify the research?
    - iii. If the study is a drug, biologic, or device trial, are the safety and efficacy data sufficient to warrant the proposed phase of testing?
  - **Background and Expertise of Study Team**

- i. Is there sufficient expertise on the research team to conduct the study given the procedures and the study population(s)?
  - ii. Are the researchers' experience, specific roles and responsibilities clearly defined?
  - iii. Have any conflict of interest issues disclosed been addressed with a management plan?
- **Research Methodology/Study Procedures**
  - i. Are the scientific design and research procedures adequately described and justified? Is the design appropriate to answer the research question? (Scientific merit should be considered in the context of whether individuals should be exposed to unnecessary risk).
  - ii. Does the description differentiate between standard-of-care procedures and research procedures, if applicable?
  - iii. Elements of the research design that need special attention include placebo control, washout periods, deviations from accepted standards of care, etc. Does the researcher provide adequate justification for these elements?
  - iv. If drug, biologic, or device trial...
    - Is the status of the drug or device described (i.e., experimental)? Does the application include the FDA IND/IDE number?
    - Are the dosage and route of transmission justified and appropriate?
    - Is the significant or non-significant status of the device justified and appropriate?
- **Subjects (participants, charts, records and/or specimens)**
  - i. Is the proposed subject population appropriate given the research question?
  - ii. Are the inclusion and exclusion criteria explained and appropriate?
  - iii. Is the inclusion or exclusion of women, minorities, and minors justified?
  - iv. Does the proposed population include vulnerable participants (e.g., minors, prisoners, cognitively impaired, ECU/UHS students/staff)? If yes, consider special protections (e.g., parental permission, minor assent, surrogate consent, minimize undue influence or coercion to ensure voluntariness).
  - v. Does the researcher include a projected sample size and appropriate justification? Is the projected sample sufficient to answer the research question, yet small enough to limit number of individuals placed at risk?
- **Recruitment/Informed Consent Process:** Are the recruitment procedures clearly described?
  - i. Are the location and timing of the recruitment procedures appropriate considering the proposed populations?

- ii. Are the recruitment procedures appropriate (ensure that they do not violate an individual's right to privacy)?
  - iii. Is the informed consent process sufficiently described?
  - iv. If recruiting minors, does the researcher address parental permission and minor assent procedures?
  - v. If recruiting elderly subjects or potentially cognitively/emotionally impaired groups, does the researcher explain how competency will be determined and who will make the determination?
  - vi. Is the researcher requesting to obtain surrogate consent? Does the researcher adequately justify use of a surrogate? Does the researcher have a specific plan that will be employed to acquire and document surrogate consent? Is the plan appropriate?
  - vii. If recruiting minority groups or non-English speakers, does the researcher acknowledge that s/he will obtain informed consent or assent using a consent/assent form translated into the appropriate language?
- **Anticipated Risks/Risk Management**
  - i. Are the potential risks sufficiently identified, evaluated (probability and severity) and described?
  - ii. Are the risks minimized to the lowest level possible?
  - iii. After reviewing potential direct benefits to the participant and societal benefits, are the risks appropriate in relation to the anticipated benefits?
  - iv. If research includes vulnerable populations (e.g., minors, pregnant women, prisoners) determine which regulatory category of risk the research falls within and whether all the criteria within the category or Subpart are addressed?
- **Potential Benefits** - Are the potential benefits (to participant and society) sufficiently identified, evaluated and described?
- **Adverse Event Reporting/Management**
  - Is there a data safety monitoring plan or board/committee in place?
  - Does the protocol specify criteria for stopping (for a subject or for the project)?
  - Does the researcher acknowledge that the research team will follow ECU's reporting policy on Unanticipated Problems?
- **Costs** - Is there sufficient justification for the participants to pay for costs associated with protocol (e.g., charge for standard-of-care procedures, FDA-approved device charge, parking fee, etc.)?
- **Compensation**
  - Is the amount and type of compensation reasonable (does not appear to unduly influence one to participate)?

- Does the researcher explain that compensation will be prorated and provides a schedule of payment?
    - **Privacy and Confidentiality Of Research Data**
      - Are there appropriate procedures in place to protect the participant's privacy?
      - Does the researcher explain who will have access to the data?
      - Are the security procedures regarding access and storage of the data adequate?
      - Is the use of personal identifiers or codes linking the data to the participant justifiable? If yes, does the researcher explain at what point the data will be de-identified?
3. **Read the supporting documents (e.g., Investigator's Brochure, protocol, grant application, surveys, recruitment materials, etc.).**
- *Investigator's Brochure* provides the reviewer background information (animal data; preliminary human studies) about the investigational drug, biologic, or device.
  - *Protocol* provides a detailed description of study procedures including a power analysis justifying projected sample size, and the statistical methods to be used to analyze the data.
  - *Grant application* - Does the IRB application match the grant application?
  - *Recruitment materials/advertisements* should be in lay language and describe the study to potential participants.
    - **SHOULD INCLUDE** – Name of Institution and department; Name of researcher and contact person along with contact information; state that the study is “Research”; purpose of research study; inclusion/exclusion criteria; procedures and time commitment involved; compensation and location of research.
    - **SHOULD NOT INCLUDE** – emphasis on monetary compensation; misleading or exculpatory language; emphasis on "free" services (e.g., medical care).
4. **Re-read the consent document.** Make changes or note questions for the researcher to address.
5. **Read the Reviewer Checklist:** Write comments and recommendations on Reviewer's checklist and be prepared to present them to the Committee.

\* Adapted from "Institutional Review Board Member Handbook"  
by Robert Amdur, MD  
Jones and Bartlett Publishers, 2003

### **OHRP §45CFR46.115(a)(2)**

Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

**FDA 21CFR56.115(a)(2)**

Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.