The 111 Criteria: What it takes to get your study approved

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Belmont Principles

- Beneficence
- Respect for persons
- Justice

The regulations were written to operationalize these principles

Criteria for Approval (aka .111 criteria)

- In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(If the IRB cannot make these determinations the proposal cannot be approved. It can be disapproved, deferred or “conditionally” approved.)

Deferral vs. Conditional Approval

- When the Board cannot determine that all of the criteria are met, they cannot approve the research. It is deferred and the investigator is asked to make modifications or provide additional information.
- When the Board can determine that all of the criteria are met provided specific changes are made, the Board can conditionally approve the research. However, final approval requires that the specific changes have been made and this is confirmed by the Chair or chair designee.

First Criteria

- 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

  – What Principle: Beneficence, Respect or Justice

Unable to determine risks are minimized

- An outcome measure (in a drug study for pulmonary hypertension) was change in pulmonary artery pressure measured during right heart catheterization (RHC). If patients had a RHC for clinical care within 30 days of enrollment, the study required only one study driven RHC. If they had a RHC more than 30 days prior to enrollment, the study required 2 RHCs. The Board tabled the protocol and asked the Investigator would it be possible to do the study using only subjects who had a RHC for clinical care.

- If the study could be designed in this way, the risks of the research would be further minimized.

Second Criteria

- 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)

  – What Principle: Beneficence, Respect or Justice

Unable to determine risk: benefit ratio

- In one study an exclusion criteria was “No contra-indication for oral radiology and dental examination”
  - Neither the protocol nor the consent form mentioned X-rays
- If X-rays were part of the research, the risk to subjects is greater than if they were part of standard of care.
- Deferred because this determination of risk benefit ratio could not be made without this information.

Third Criteria

- 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, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

  – What Principle: Beneficence, Respect or Justice

Inequitable selection of subjects

- A study that had been open at several US sites for a number of years with poor enrollment, proposed adding two sites in India “because we are confident that we can rapidly enroll there.”
- Targeting a vulnerable (poor) population for convenience violates the principal of Justice an the regulatory requirement for equitable selection of subjects.

Fourth Criteria

- 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 §46.116.

  – What Principle: Beneficence, Respect or Justice

Inadequate provision for Informed Consent

- Countless studies are deferred because of deficiencies in the consent form (the required elements of consent can be the subject of another talk)
- Consent can be waived, but it must meet specific criteria. The most important one being that it is impracticable to obtain consent - not just difficult.

Fifth Criteria

- Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

  – What Principle: Beneficence, Respect or Justice

Inadequate documentation of Informed Consent

- This is rarely a reason for deferral. Sometimes the investigator wanted to waive DOCUMENTATION of consent, but failed to explain how the study met the criteria for waiver of DOCUMENTATION.

Sixth Criteria

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

  – What Principle: Beneficence, Respect or Justice

Inadequate plan to monitor the data

- The purpose for having a DSM Plan relates to the need to monitor what is happening in the study so that if something untoward is happing, it is recognized and changes are made to protect subjects. The most common reason for deferral is the absence of a plan.
- Sometimes, for particularly risky studies, the IRB may require establishment of an independent board that has a defined plan to monitor the study.

Seventh Criteria

- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

  – What Principle: Beneficence, Respect or Justice

Inadequate plan for privacy and confidentiality

- In a chart review study, the Investigator stated "Study data will contain medical record numbers. We will maintain the confidentiality of data and privacy of subjects."
- The IRB has to determine if the proposed method for achieving this is adequate.

Extra Criteria

- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

  – What Principle: Beneficence, Respect or Justice

Inadequate protections for vulnerable people

- A study proposed to enroll subjects into a moderately high risk protocol and to enroll non-English speaking subjects using the “short form” consent process.
- The Board deferred the protocol until the Investigator provided a plan for how to respond to subject concerns or problems during off hours.

Requirements for Approval (for all studies)

- Risks to subjects are minimized
- Risks to subjects are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent will be sought
- Informed consent will be appropriately documented

Requirements for Approval (when appropriate)

- The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- 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 additional safeguards have been included.

It couldn’t be easier

Thank you