Categories of Action: Criteria for Approval

(a) In order to approve research covered by this policy the IRB shall 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, pregnant women, mentally disabled persons, 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 §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 46.117.

(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.

(b) 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.

Categories of Action: Initial Review (Policy RR 407)

The IRB may make one of the following determinations as a result of its review of research submitted for initial or for review:

Approval

When an acceptable risk/benefit ratio exists and the criteria required for approval are deemed acceptable, protocol is approved as submitted.

Withheld Approval Pending Changes
The IRB determines that the protocol will meet the regulatory criteria for approval provided the investigator agrees to make specific changes to the IRB application including the informed consent document.

Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB Executive Chair, Chair or another designated IRB member subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure.

Research may not be initiated until a letter of IRB approval is received and other applicable committee reviews are satisfied.

**Tabled**

The IRB requires substantive changes that are directly relevant to the determinations required by the IRB under federal regulations at §.111, the IRB will table the approval of the protocol pending subsequent review by the convened IRB of the responsive material.

**Disapproved**

The IRB determines that the research does not meet the regulatory criteria for approval and cannot provide modifications that may allow the protocol to be approved.

<table>
<thead>
<tr>
<th>Categories of Action: Continuing Review (including modification) {Policy RR 407}</th>
</tr>
</thead>
</table>
| **Approval**  
When an acceptable risk/benefit ratio exists and the criteria required for approval are deemed acceptable, protocol is approved as submitted.  

**Conditional Approval**  
When the IRB determines requires minor modification to the protocol or accompanying documents.  

**Suspension**  
Study is suspended pending further clarification of issues that deal with the criteria at §.111.  

<table>
<thead>
<tr>
<th>Withheld Approval Pending Changes vs. Tabled</th>
</tr>
</thead>
</table>
| **WITHHELD APPROVAL PENDING CHANGES** When the IRB votes to WITHHOLD APPROVAL PENDING CHANGES, an IRB chair or experienced IRB reviewer may approve the changes using an expedited mechanism. When the IRB withholds approval, the IRB should have in mind a clearly defined protocol that it is willing to approve. This protocol does not exist in final form, but represents the submitted protocol with specific required modifications. The IRB should document the required modifications so that an IRB chair or experienced IRB member can judge whether the revised protocol matches the one the IRB was willing to approve.  

The IRB should provide the investigator specific modifications required to secure approval. For example,  
✓ “Participants must be 18 years or older”  
✓ “Drop the placebo controlled arm of this study”  
✓ “Offer psychological counseling to all participants at the study's conclusion”  
✓ “Require CAT scans every three months”  
✓ “Require the data and safety monitoring board to meet every three months”  

5 May 2009
✓ "Include in the consent all side effects listed in the investigator's brochure"

The IRB may be less specific provided the modifications may be reviewed by the expedited procedure. For example, "Rewrite the content of the consent into lay language," or "Modify advertisements according to IRB policy" or "Submit quality of life surveys for review."

**TABLED**
The IRB should not grant withheld approval if the judgments of the convened IRB are required for any of the criteria that the IRB must consider for approval. Such requests would include:
✓ "Explain why participants less than 18 years of age will be allowed to participate"
✓ "Provide additional justification for the use of placebo"
✓ "Clarify whether participants will be offered counseling services at the end of the study"
✓ "Indicate how often the data and safety monitoring board will meet"
✓ "Provide additional animal data for the study drug"

### Regulations and Regulatory Guidance

- 45 CFR §46.110
- 21 CFR §56.110
- AAHRPP Accreditation Standard II.2.B
- Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure
- OHRP Compliance Activities: Common Findings & Guidance #6, #21, #71
- OHRP Guidance on Expedited Review
- FDA Information Sheets: Continuing Review after Study Approval

**Example of OHRP Compliance Finding**

"OHRP finds that the IRB occasionally approves research contingent upon substantive modifications or clarifications without requiring additional review by the convened IRB. For example, in the 12-16-03 review of protocol #M11047-101, the IRB approved the protocol contingent upon information about the randomization process, services that suicidal subjects would receive, exclusion of pregnant women, and how stigmatization might affect family and community relationships."