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Subject: Types of IRB Review
Division: IRB
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IRB Policy 105.5: FULL BOARD REVIEW

Policy

Full IRB review is required for most new applications submitted for review and approval. It is also required for most protocols seeking renewed approval as well as for many amendments.

The convened meetings are generally held once every four to six weeks. A necessary quorum for the IRB to consider a proposal is a majority of the total membership, including a member whose primary concern is in a nonscientific area, before official actions may be taken at these meetings. The IRB will not have a member participate in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB. An IRB member with a potential or real conflict of interest will leave the room during discussion and voting and the recusal will be noted in the IRB meeting minutes.

Appropriate Board members will be assigned by the IRB Chairperson and/or Administrator to be principal reviewers on one or more of the applications, for research involving vulnerable subject populations, and for continuing reviews. In cases where it is deemed necessary, consultants to the IRB may be asked to comment on a proposed research activity. Consultants will receive all of the same information that the IRB received, regarding the particular protocol, and will either be present at the meeting or provide a report to the IRB to be reviewed at the meeting.

When FDA-regulated research is reviewed, there shall be one member, or a consultant, who is a physician present, or the report of this member/consultant should be reviewed/discussed. If the IRB has any question for this member/consultant who is not present, the research will not be approved until the question has been answered to the IRB's satisfaction.

Voting

The IRB may take the following actions after review of the protocol and the informed consent document:

1. Unconditional Approval
2. Contingent Approval
3. Deferred
4. Tabling
5. Disapproval

Unconditional Approval

The IRB may approve a protocol/continuing review/amendment, etc. unconditionally and the study may begin/continue immediately after approval. In accordance with 21 CFR 56.111 and 45 CFR 46.111, the IRB has to 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 21 CFR 50.20 and 45 CFR 46.116.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 21 CFR 50.27 and 45 CFR 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.

8. 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

Contingent Approval

The IRB may approve research with conditions if, given scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval under the HHS regulations at 21 CFR 56.111 and 45 CFR 46.111. If the IRB is able to specify changes to the research protocol or informed consent document, or seek clarification of specific facts, that if made or provided would enable the IRB to make the required determination(s), then approval with conditions would be permissible.

The IRB may require the following as conditions of approval of research:

1. Submission of clarification of facts (e.g., clarification that the research excludes children);
2. Submission of additional documentation (e.g., certificate of ethics training);
3. Precise language changes to protocol or informed consent documents; or

4. Substantive changes to protocol or informed consent documents along with clearly stated parameters that the changes must satisfy.

When the IRB approves research with conditions, verification procedures must be included as part of the IRB approval process, under which the IRB chairperson (and/or other individual(s) designated by the IRB) will review responsive materials from the investigator required by the IRB, and determine whether the conditions of approval have been satisfied. The IRB's verification that the investigator has satisfied all conditions of approval stipulated by the IRB helps to ensure that the investigator does not initiate any research that is different from what was approved by the IRB.

Examples of changes or clarifications that illustrate the types of conditions that an IRB may require when granting contingent approval:

1. Requiring submission of documentation of an endorsement letter from a department chair, as required by institutional policy;
2. Requiring correction of minor grammatical and typographical errors in the informed consent document;
3. Requiring that a listed investigator provide a copy of his approved clinical privileges/hospital staff appointment document in order to confirm that he has approval to perform the type of clinical procedure proposed in the research protocol at the institution where the research is to be conducted;
4. Requiring that the investigator re-locate in the informed consent document the statement "You will receive $500 for participating in this study" from the "Benefits" section of the form to a separate section under the heading "Compensation,";
5. Requiring that the investigator add "a history of aspirin use in the past 14 days" to the exclusion criteria for subject enrollment in the research protocol;
6. Requiring the investigator to (a) confirm that any standard contrast material used in radiological procedures dictated by the research protocol will be limited to agents and dose levels specified in precise detail by the IRB, and (b) submit a revised protocol which includes the precise agents and dose levels;
7. Requiring that the investigator modify the informed consent document to include standard template language used for research involving college psychology students, stating that comparable non-research alternatives for earning extra credit will be offered to students who choose not to participate in the research;
8. Requiring the addition to the informed consent document of a description of the risks of a standard chemotherapy drug, where the risks are well-described in the research protocol;
9. Requiring simplification of the description of the study risks in the informed consent document to be at an 8th grade comprehension level;
10. Requiring that the research protocol be revised to include a plan for (a) informing subjects about the results of standard cardiac function tests dictated by the research protocol, and (b) referring subjects for appropriate clinical follow-up.

Deferred

The IRB may defer approval if the IRB specifies conditions under which research can be reconsidered for approval, pending substantive (i.e., directly relevant to the IRB determinations required under 45 CFR 46.111 and/or 21 CFR 56.111) clarifications or modifications to the protocol and/or informed consent process/document. Research activity may not commence until the investigator has provided the information, clarifications or revisions, and the IRB has reviewed and approved the response at a convened meeting.

For example, the IRB cannot approve a proposed research project undergoing initial review when the IRB (a) is unable to make the required determinations about research risks and benefits, the adequacy of privacy and confidentiality protections, or the adequacy of the informed consent process because the

research protocol provides insufficient information related to these aspects of the research, and (b) is unable to specify changes to the research protocol that if made would allow the IRB to make these required determinations.

When an IRB reviewing a research project at a convened meeting is unable to approve research because it cannot make the determinations required for approval, the IRB can either disapprove the project, or defer the project for further review at a future date. When deferring the project, the IRB, under its authority to require modifications in order for an investigator to secure approval, may require that the investigator (a) make changes to the protocol, (b) make changes to the informed consent documents, (c) submit clarifications, and/or (d) submit additional documentation.

Examples of required changes or clarifications that generally would preclude the IRB from approving the research include the following:

1. Providing a justification for using a placebo and withholding known effective treatment for a serious medical condition for subjects assigned to a control group;
2. Providing a justification for enrolling children in the research and an explanation of how the research would satisfy the requirements of subpart D of 45 CFR part 46;
3. Revising the study hypothesis and, accordingly, the study design;
4. Providing a description of procedures that the control group will undergo; or
5. Providing a plan to implement additional subject monitoring in order to reduce risks to subjects, given the number of serious adverse events that have occurred in study subjects since the prior IRB review.

Tabling

The IRB may table a protocol if review was not initiated or was not completed, resulting in postponement of convened IRB review, usually due to loss of quorum, pertinent documents are unavailable or the scope of IRB expertise is not considered sufficient for appropriate decision-making.

Disapproval

The IRB may disapprove a protocol when the determinations required for approval of research cannot be made, even with substantive clarifications or modifications to the protocol and/or informed consent process/document. The project does not meet the criteria for approval and there are serious concerns related to one or more criteria.

Minutes

Minutes, in sufficient detail to reflect the names of the committee members that are present, the action of the committee on each protocol on the agenda, all restrictions, conditions, modifications or additional information requested for each protocol, major issues discussed, and the rationale for each disapproval, will be taken at all IRB meetings. At the convened meeting each submission is discussed and a vote is taken. The IRB minutes will be written by the Administrator and approved by the IRB Chairperson within seven business days of the meeting date.

Investigator Responses

The IRB Chairperson will inform the investigator in writing of the decision of the Board, within ten business days of the meeting. If changes are recommended by the board, the IRB Chairperson will communicate these in writing to the investigator.

If a response from an investigator to an IRB letter requesting additional information is not received within

three months, the investigator will be sent a notice stating that the protocol application has been administratively withdrawn from consideration. Once it has been administratively withdrawn due to lack of response, the review may be continued only upon receipt of a formal letter requesting reactivation and addressing the concerns raised in the initial review. The new material will then be reviewed by the full Board at the next committee meeting.

Adverse decisions may be appealed by re-review of the proposal. Appeals will be heard only when the proposal has been revised and/or provides additional information.

Responsibility

IRB Administrators are responsible for ensuring that IRB reviewers have the tools they need to complete their research reviews. IRB Reviewers are responsible for conducting a thorough review and making all appropriate approval recommendations for consideration by the IRB.

Applicable Regulations and Guidelines

45 CFR 46.108, 46.109
21 CFR 56.108
NIH IRB SOPs
OHRP Guidance on IRB Approval of Research with Conditions (November 10, 2010)