IRB Policy 9: Full Review Policy
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I. Pertinent Definitions:

A. **Continuing Review:** periodic IRB review of ongoing research activities to ensure that the rights and welfare of human subjects are protected. Includes analysis of risk/benefit ratio, with special attention to whether new information or unanticipated risks have been discovered since the previous IRB review, and whether any new information regarding the risks and benefits should be provided to participants.
B. **Exempt Review:** Studies determined by the IRB to meet the exempt criteria as defined by the Federal regulations. Exempt studies do not require periodic review by the IRB unless a change in the project is planned.
C. **Expedited Review:** Studies determined by the IRB to meet the expedited criteria as defined by the Federal regulations.
D. **Initial Review:** Studies presented for review prior to project initiation
E. **Full Review:** Studies determined to require review by convened IRB

II. Summary Policy

The policy of both the East Tennessee State University Campus Institutional Review Board (ETSU IRB) and the East Tennessee State University/ Veterans Affairs Institutional Review Board (ETSU/VA IRB) is to receive and review sufficient information to make the determinations required for approval of research under HHS Regulations at 45 CFR 46.111. This includes sufficient information about recruitment and enrollment procedures, the equitable selection of subjects, provisions to protect the privacy of subjects and maintain the confidentiality of data, and additional safeguards to protect the rights and welfare of subjects who are likely to be vulnerable.

III. Review Category- Initial Full Reviews

A. Covered Activities

In accordance with HHS Regulations at 45 CFR 46, the IRB must review and approve all non-exempt human subject research covered by an assurance. The Principal Investigator (PI) may request a certain type of review (i.e., expedited

review) but the final determination is made by the IRB. Studies not qualifying under expedited or exempt criteria must be reviewed by the full, convened board.

B. Investigational New Drug

Protocols involving an Investigational New Drug must be submitted with an appropriate IND number (indicating FDA approval). Under no circumstances will an investigational drug protocol be accepted for review prior to its having received an IND number.

C. Primary Reviewers

To improve the quality and efficiency of IRB review, the Primary Reviewer system will be used to conduct initial review of proposals presenting more than minimal risk. Under this system, a minimum of two members will be assigned to each protocol to be reviewed at the full-committee meeting. Each initial full review is assigned a Primary Scientific Reviewer and a Primary Informed Consent Reviewer. The assigned Primary Scientific Reviewer will have scientific or scholarly expertise in the area of the research adequate to the complexity and scope of the research. A Primary Informed Consent Reviewer will also be assigned for each initial full review.

Primary Reviewers shall be IRB members who are appointed each month to the task by the IRB Chair. Selection is based on consideration of the protocol and reviewer's area of expertise, dedication to continuing education and availability to accept new and continuing research. The IRB Chair will sign the xform 115 for IRB Chairs documenting reviewer assignments, including designation of any consultants as deemed necessary.

1. The Primary Scientific Reviewer conducts an in-depth review of protocol and other pertinent documentation prior to the IRB meeting. Issues to be analyzed include, but are not limited to, scientific merit and the risk/benefit ratio. The reviewer then presents a summary of the study to the full IRB, with any recommended modifications.

2. The Primary ICD Reviewer conducts an in-depth review of the Informed Consent Document and associated documents (i.e., Child Assent, HIPAA authorization). The reviewer then presents his/her ICD assessment and any recommended modifications to the full IRB.

3. Both the Primary Scientific and ICD Reviewer may contact the Principal Investigator prior to the IRB meeting to request additional information if necessary. The IRB members will have access to any additional

information provided to Primary Reviewers. Primary Reviewer's participation shall be noted in the minutes for each proposal review.

D. Materials to be reviewed by the Primary Reviewer (Scientific)

The following materials are provided to the Primary Reviewer approximately 10 days prior to meeting. The primary scientific reviewer is expected to review these materials:

a. Xform new protocol submission xform, which includes the narrative section, and any attached documents such as MSHA Research Request Form
b. full protocol
c. proposed informed consent document
d. any relevant grant application
e. investigator's brochure, if there is one
f. any recruitment materials, including any advertisements intended to be seen or heard by potential participants
g. for HHS supported multicenter clinical trials, a copy of the HHS approved sample informed consent document*
h. for HHS supported multicenter clinical trials, a copy of the complete HHS approved protocol
i. Investigator CV
j. any advertisements, questionnaires, surveys, testing forms and/or introduction letters associated with the study and intended for participant use or view
k. any consultant's report (if available at time of agenda generation
l. for studies that have an associated contract, verification from Sponsored Programs of the consistency for provisions of medical care or other care and services for research-related injury between the consent document and the contract

* Any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample ICD must be justified in writing by the investigator, approved by the IRB, and reflected in the IRB minutes.

The Primary ICD reviewer is responsible for reviewing the above documents with the exception of the investigator's brochure.

The Primary Reviewer performs an in-depth review of all documentation and completes the xform 111 to provide documentation of consideration of required elements for study approval. The Primary ICD reviewer also completes the required sections of the Form 111 xform.

E. Materials to be reviewed by all other IRB members:

Approximately ten days prior to the meeting, all other IRB members are provided access to and are expected to review:

a. Xform new protocol submission, which includes the narrative section, and any attached documents such as MSHA Research Request Form
b. proposed informed consent document
c. any recruitment materials, including any advertisements intended to be seen or heard by potential participants
d. Investigator CV (if new investigator)
e. Any advertisements, questionnaires, surveys, testing forms and/or introduction letters associated with the study and intended for participant use or view
f. Any consultant's report (if available at time of packet distribution)
g. for HHS supported multicenter clinical trials, a copy of the HHS approved sample informed consent document*
h. for HHS supported multicenter clinical trials, a copy of the complete HHS approved protocol

In addition, consultant's reports are forwarded to all IRB members in the electronic system or per email per Policy 4, Section III.
Upon request, any IRB member has access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting. In addition, any IRB member has access to additional information provided to individual reviewers.

F. Convened Meetings

Applications for consideration at the convened meeting of the IRB shall be made available to the Primary Reviewers and the members of the IRB 10-14 days prior to the convened meeting. Members with a vested interest in any protocol may not participate in the deliberation and voting process, although these members may participate in the discussion of such proposals to provide information requested by the IRB.

Initial full reviews will be individually presented, and discussed by the IRB as a whole group. Approval will only be granted after substantive review and careful consideration of the determinations required under HHS Regulations at 45 CFR46.111. Any controverted issues and their resolution will be documented in the minutes.

G. Initial Full Reviews

Initial reviews of research must be conducted by the IRB at convened meetings at which a majority of the members are present, including at least one member

whose primary concerns are in the non-scientific areas, except where expedited review is appropriate under HHS Regulations at 45 CFR 46.110(b)(1) for the categories of research listed in the Federal Register of November 9, 1998. Approval of research is by a majority vote of this quorum.

In conducting the initial review of proposed research, the IRB will obtain information in sufficient detail to make the determinations required under HHS Regulations at 45CFR 46.111. IRB members receive the materials sufficiently in advance of the meeting date to allow review of the material.

H. Presentation by PI

The Principal Investigator will be asked to attend the meeting in which his/her proposal will be discussed. If the investigator cannot attend the meeting, a qualified, knowledgeable representative (e.g., M.D. or Ph.D. for medical protocols) may be sent. In the event of a study being presented by a thesis / dissertation student, the student's (knowledgeable) advisor or faculty co-investigator should attend the meeting to support the presentation of the protocol alongside his/her student as well. When a student is indicated as the Principal Investigator, a faculty member must be identified as a Co-investigator. The IRB members are encouraged to ask the investigator for a synopsis of the research and to explain or clarify points that bear on the risk/benefit ratio or to supply missing materials.

I. Committee Responsibilities

The full IRB Committee is informed of the Primary Reviewer's findings during the convened meeting. At the meeting, following the investigator's presentation, the Primary Reviewers will initiate discussion by presenting an overview of the goals, design, study procedures and safety procedures for each study. Particular attention will be paid to the Risk/Benefit Ratio of the investigations and the adequacy of the Consent Forms in conveying the procedures, implications and full intent of each study. Problems identified by the Primary Reviewers or by other IRB members will be discussed and suggestions for any necessary changes will be agreed upon by the IRB.

The Primary Reviewer may present findings and recommendations regarding initial or continuing review in the presence of the PI or once the investigator has been excused from the meeting (along with any IRB member(s) declaring association or other conflict of interest).

The responsibilities of the IRB members include: reviewing the investigator's curriculum vitae (to confirm the qualifications of the investigator and confirm research experience), reviewing the new protocol submission xform, consent

document, scientific review of the protocol, and (if applicable) the investigator brochure, the associated grant application, questionnaires, and advertisements to discuss these items at the meeting, and to vote on the proposal. In instances where the IRB determines their expertise as not sufficient to review adequately the technical aspects of the study, outside consultants may be used. These consultants may be present for the discussion of the study, but will be excused during the deliberation and voting process. The OPHRS staff will be responsible for assisting the IRB Chair and members by serving as the liaison between the IRB and the investigator.

If the study involves vulnerable populations, the IRB is responsible for determining if additional safeguards need to be in place to protect the rights and welfare of these vulnerable subjects.

In conducting the full IRB Committee review, the majority of the members must agree that sufficient materials are present to determine that the study meets criteria 45 CFR 46.111 and if applicable, 21 CFR 56.111 or 38 CFR 16.111 for approval.

For studies subject to the 1991 Common Rule and FDA rules,

(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 by: (a) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (b) 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 appropriate federal and state regulations and institutional policies and procedures.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by appropriate federal and state regulations and institutional policies and procedures.

(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 research is more than minimal risk and involves an intervention

(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.

When the revised Common Rule is in effect, for studies subject to the revised Common Rule,

(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 by: (a) by using procedures that are consistent with sound research design and that do not unnecessarily expose

subjects to risk, and (b) 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. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or 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, § __.116

(5) Informed consent will be appropriately documented or appropriately waived in accordance with § __.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.

*When research is more than minimal risk and involves an intervention; not applicable for expedited studies

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

For all:
When appropriate, the Informed Consent Document should include the additional elements of informed consent (refer to Informed Consent policy).

The patient's medical record must be flagged if study is determined to be more than minimal risk.

If the IRB determines and documents that the patient health record must be flagged in Computerized Patient Record System (CPRS) as participating in a research study, then the health record must identify the Researcher, as well as contact information for a member of the research team that would be available at all times, and contain information on the research study or identify where this information is available. The duration of flagging is the length of the duration of the individual's participation in the study.

The instructions above apply to studies that **do not** have a Certificate of Confidentiality. Refer to Policy 13, Section VIIIC for instructions regarding studies that DO have a Certificate of Confidentiality.
After review, the possible actions which may be taken by the IRB are:

- Approval of the proposal
- Approval with stipulations
- Defer pending receipt of additional information
- Disapproval

Motions are made, and votes taken on such motions, only in the absence of the investigator and those IRB members with vested interest in the protocol. Voting is by voice or raised hands unless a secret ballot is requested by any IRB member. The staff records all votes. The minutes will record those IRB members who are in attendance at the meeting but are absent from the room at the time of vote. The recording of votes will denote the number of votes for, opposed, abstained and recused.

J. <u>Approvals:</u>

If the proposal is approved or approved with stipulations, members also decide on the interval for the ongoing review of the study based on the degree of risk to human subjects. Continuing reviews for approval beyond the initial year will be annual reviews or other predefined review periods not to exceed one (1) year. The criteria as specified in Policy 11 are considered when determining the review interval for full studies.

If the proposal is approved with stipulations that require simple concurrence by the investigator, the OPHRS staff informs the investigators of the stipulations and

the actions required by the investigator to satisfy them. If the convened board stipulates certain provisions requiring simple concurrence by the investigator, the IRB Chair or another IRB member designated by the Chair may subsequently approve the revised protocol on behalf of the IRB under an expedited review procedure. The Chair's expedited approval of research contingent upon specific minor conditions will be placed on the agenda and documented in the minutes of the first IRB meeting after the date of the approval. If necessary, response to stipulations may be submitted to the full IRB for reconsideration.

Upon subsequent approval of protocols by the full IRB, Chair, or Secondary Reviewer, a letter subsequently informs the investigator of the determination/action of the IRB, including the determined period of continuing review. The IRB coordinator will release approvals for the protocol only after the required changes have been made, received by the IRB Office, and approved as indicated above. See Procedure 9a for description of posting of documents in IRBManager.

The approval letter(s) instruct the PI that any changes in approved projects must be reviewed and approved before they are initiated; that any unanticipated problems, deaths or other adverse event must be reported to the IRB; and that monitoring will occur. The frequency of monitoring will be determined by the IRB at the time of initial or continuing review (as noted above and in continuing review policy), and investigators will be informed of this period.
Upon study approval (except in cases of waiver), the IRB Coordinator is responsible for posting an approved copy of the Informed Consent document in IRBManager for studies. Each page of the Consent will bear an IRB stamp of approval and expiration date over the initials of either the IRB Chair, Vice Chair, Director or IRB Coordinator. For non-VA studies, the IRB Coordinator will post the stamped approved consent document as an attachment on the "New Protocol Submission" event and on the protocol page (Attachment Section). For VA studies, the IRB Coordinator will post the informed consent document as an INTERNAL ONLY attachment on the "New Protocol Submission" event and on the protocol page (Attachment Section) in IRBManager. When VA R&D approval is verified by the IRB, the IRB Coordinator will remove the "Internal only" status so that the informed consent document is visible to study staff.

The approved ICD must have a version date and an area for the subject to initial each page of the ICD in the footer area. Particularly for ICDs used in medical research, the IRB may recommend that the *time* of participant signature be added to signature area of the consent document. See Procedure 9a for description of posting of documents in IRBManager.

K. Deferral Pending Receipt of Additional Information

When the convened board requests substantive modifications or clarifications regarding the protocol or informed consent that are directly relevant to the determinations required by the IRB approval of research under HHS Regulations at 45 CFR 46.111, IRB approval of the proposed research is deferred, pending subsequent review by the convened board of responsive material. The investigator will receive a written request for specific or additional information required.

Approval of the project will not be granted until all deficiencies are corrected to the satisfaction of the IRB. The IRB may request that an outside consultant review the application.

L. **Disapproval**

In the event that a proposal is disapproved at the meeting, the investigator will be notified in writing of the Board's disposition along with an invitation to respond either in person or in writing. The appeal process will additionally be made available. The investigator may alternately choose to represent the protocol rather than appeal.

References:

45 CFR 46.111
OHRP Compliance Activities: Common Findings and Guidance
63 FR 60634-60637
4 CFR § 46.107(f)
21 CFR § 56. 107(f)
VHA Directive 1200.05