CHAPTER 4 – IRB Review: Exempt, Expedited, and Full

All research involving humans that falls under the jurisdiction of the IRB for review and approval must meet the criteria for one of the following methods for review:

1) Exempt from IRB Committee Review
2) Expedited Review
3) Full Review

No human participants may be enrolled or recruited prior to receipt of written final approval of the application from the IRB for exempt, expedited and/or full reviews.

Exempt Review
Exemption does not mean “Do nothing”.

In each instance, the investigator will make the initial request for exempt status and the IRB Chair will make the final determination. If the research is submitted by the IRB Chair, the Vice Chair will review this determination.

Neither the Chair nor the Vice Chair may review for approval research studies submitted for exempt or expedited review from their respective departments or divisions (for larger departments. The exemption status must be approved by the IRB Chair or an experienced IRB member designated by the Chair. If upon this review the determination of exemption is not upheld, the investigator will be informed and provided with the reasons for denial of exemption. The protocol may then be submitted for either expedited or full review, as appropriate to the level of risk, to the IRB.

The institution retains the option under the assurance to not claim the options provided for exempt status, but instead choose to require IRB review.

Documentation for all exemptions will include citation of the specific category justifying the exemption.

Research that is determined to be exempt from IRB review is not exempt from protection of human subjects. All exempt research is subject to human subject protections and ethical standards. In addition, when the revised Common Rule goes into effect, the IRB will conduct a limited review of the research as required.

Categories for Exempt Approval:
Under the 1991 Common Rule, only studies that meet one or more of the six categories of exempt activities as delineated by DHHS Regulations (45 CFR 46 (101)(b) are eligible to be given exempt status. NOTE: These categories do not apply to prisoners and categories 1-5 do not apply to FDA regulated research.
When the revised Common Rule goes into effect, for studies subject to the Common Rule:

1) Only research activities in which the only involvement of human subjects will be in one or more of the six specific categories of exempt activities as delineated by HHS Regulations 45 CFR 46 (1041) (db) are eligible to be given exempt status. ETSU has determined to not allow exemptions under category 7 or 8.

2) Categories 1-5 and 7-8 do not apply to FDA-regulated research.

3) Subpart B (pregnant women, fetuses and neonates): Each of the exemptions at this section may be applied to research subject to subpart B if the conditions of the exemption are met.

4) Subpart C (prisoners): The exemptions at this section do not apply to research subject to subpart C, except for research aimed at involving a broader subject population that only incidentally includes prisoners.

5) Subpart D (children): The exemptions at paragraphs (d)(1), (4), (5), (6), (7- not allowed at ETSU), and (8- not allowed at ETSU) of this section may be applied to research subject to subpart D if the conditions of the exemption are met. Paragraphs (d)(2)(i) and (ii) of this section only may apply to research subject to subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Paragraph (d)(2)(iii) of this section may not be applied to research subject to subpart D.

6) Transnational: Laws and regulations in some countries do not allow exemptions. If the research is not eligible for an exemption under the laws of that country, even though the research may be covered by DHHS regulations, ETSU will not allow an exemption for research.

For a list of the categories that qualify for exempt approval, check the IRB website at [www.etsu.edu/irb](http://www.etsu.edu/irb).

**Ethical Standards:** Studies submitted requesting exempt status will be reviewed by the Chair or Vice Chair to determine whether the research fulfills the organization’s ethical standards. The standards are as follows:

1) The research holds out no more than minimal risk to the participants.

2) The selection of participants is equitable.

3) If the study includes recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data.

4) *When appropriate, if the study includes interactions with participants, there must be a consent process that discloses such information as:*

   a) that the activity involves research

   b) a description of the procedures

   c) that participation is voluntary
the name and contact information for the investigator

*When appropriate: always applies unless the IRB Chair determines that this requirement is not applicable.

The IRB Chair may determine that this requirement is not applicable if both of the following criteria are true:

⇒ that omission of this requirement will not adversely affect the rights and welfare of the participants; **AND**
⇒ that the research could not practicably be carried out without omitting this requirement

If the Chair or Vice Chair identifies ethical concerns in the research submitted for exemption, the study will not be exempted.

**Confidentiality**
Studies that meet exempt criteria may still be subject to the Privacy Act. Refer to IRB Policy 14 for information regarding HIPAA.

**Procedures for Requesting an Exemption**
The following documents are required for an exempt review:

⇒ A complete new protocol submission xForm or VA new protocol submission xForm submitted through IRBManager
⇒ The xForm must include the appropriate signatures.

Attachments must include:

⇒ Copy of the final ad intended for participant view or use, if any
⇒ Copy of all research related measures (questionnaires, surveys, etc.)
⇒ Unaffiliated Investigator Form, if applicable
⇒ CV of PI
⇒ If study has an associated contract, a copy of the contract, or at minimum, a copy of any contract pages referencing provisions for medical care or other care and services for research-related injury
⇒ If the PI is a student, the xForm must include a completed Faculty Assurance Statement.

The IRB Coordinator will receive the proposed project and review for completeness, including attachments of any pertinent documents.
If any necessary documents are not present or proposed documents are incomplete, the IRB Coordinator will contact the study staff and request missing items or completion of the documents.

If documents are complete, then the IRB Chair will evaluate each proposed study and determine whether the proposed study meets exempt status.

The decision will be communicated in writing to the PI.

**Modifications**

Any proposed changes to an exempt study must be submitted to the IRB for review and approval prior to implementation. Some modifications to the research may change the review status and require the investigator to submit an application for expedited or full review. (Refer to modification policy)

**Expedited Review**

Expedited review does not mean “fast”, but rather that certain research meeting the specified criteria may be reviewed by the IRB Chairperson, the Vice Chair; or two or more IRB members who have been selected based on their expertise and experience, not at a convened Committee meeting.

**Categories for Expedited Approval**

For studies subject to the 1991 Common Rule: Only those research activities that present no more than minimal risk to human subjects AND involve only categories delineated may be reviewed by the IRB through the expedited review procedure authorized by 45.110 and 21 CFR 56.110. For a list of the categories that qualify for expedited approval, go to the IRB website.

Expedited review MAY NOT be used if:

- Research is minimal risk but does not appear in one of the listed categories
- Research involves greater than minimal risk.
- Research where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject’s financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- Research is classified and involves human subjects.

When the revised Common Rule goes into effect, for studies subject to the revised Common Rule:

HHS Regulations at 45CFR.46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register.
b)(1) An IRB may use the expedited review procedure to review the following:

(i) Some or all of the research appearing on the list described below, unless the reviewer determines that the study involves more than minimal risk;

(ii) Minor changes in previously approved research during the period for which approval is authorized; or

(iii) Research for which limited IRB review is a condition of exemption under §___.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8)

Only those research activities that

\[\Rightarrow\] present no more than minimal risk to human subjects

AND

\[\Rightarrow\] involve only procedures listed in one or more of the following categories

may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110

For research subject to the revised Final Rule, research appearing on the list of expedited review categories is deemed to be no more than minimal risk. Research that falls within the list of categories is presumed to be minimal risk unless the IRB determines and documents that the research involves more than minimal risk. If the IRB reviewer determines that the research involves more than minimal risk, it will be referred for review by the convened IRB.

Expedited review **MAY NOT** be used if:

• research is minimal risk but does not appear in one of the listed categories

• research has been determined by reviewer to involve more than minimal risk.

• research where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject’s financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

• research is classified and involves human subjects.
Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. The categories in this list apply regardless of the age of subjects, except as noted.

The IRB will apply the most current list of categories of research published in the Federal Register that may be reviewed using expedited review procedures. Refer to the IRB website for expedited categories.

Investigators should remember that even though research may be eligible for expedited review it still remains subject to the requirements of informed consent unless waived.

**Procedures Required for Expedited Review**

Because a study meeting these criteria is reviewed by the appropriate IRB Committee Chairperson, the Vice Chair, or two or more IRB members who have been selected based on their expertise and experience, there are no deadlines for submission. However, in reviewing the research, the Chairperson or designated IRB Member(s) may exercise all of the authorities of the full Committee except he or she may not disapprove the research. The Chairperson or designated Committee Member(s) may refer the application to the Committee for review or request that the study be reviewed by

The following documents are required for expedited review:

- A complete “new protocol submission xForm” or, for VA studies, the “VA new protocol submission xForm.”
- The xForm must include the appropriate signatures.

Attachments must include:

- All proposed Informed Consent Documents using the template available on the IRB website with version date as footer or header, if applicable
- Complete protocol, when applicable
- Copies of the final ad(s) intended for participant view or use.
- Copy of all research related measures (questionnaires, surveys, tests, interview question outline, including email solicitations, etc.)
- Unaffiliated Investigator Form, if applicable
- HIPPA Authorization to Use and Disclose Information Form, if applicable
- A copy of the grant application, if applicable
- CV of PI
⇒ If study has an associated contract, a copy of the contract, or at minimum, a copy of any contract pages referencing provisions for medical care or other care and services for research-related injury.

⇒ For HHS supported multicenter clinical trials, a copy of the HHS approved sample informed consent document.

⇒ For HHS supported multicenter clinical trials, a copy of the complete HHS approved protocol.

⇒ If the PI is a student, the xForm must include a completed Faculty Assurance Statement.

The IRB Coordinator will receive the proposed project and review for completeness, including attachments of any pertinent documents.

⇒ If any necessary documents are not present or proposed documents are incomplete, the IRB Coordinator will contact the study staff and request missing items or completeness of the documents.

⇒ If documents are complete, then the IRB Chair will evaluate each proposed study and determine whether the proposed study meets expedited status. The Chair and/or Coordinator will forward a copy of the proposed documents to expedited reviewers for review.

⇒ If study is approved, approved pending modifications or deferred, then the PI will be notified in writing of the decision.

⇒ If a proposed study is not approved under the expedited criteria, the PI has the responsibility to submit the study for full review, as appropriate to the level of risk, by the IRB.

**Results of Expedited Review**

Following the review by the IRB Chairperson or designated expedited reviewer(s), the investigator will receive a letter addressing one of the following possible determinations:

⇒ The study is **approved**, in which case a copy of the consent documents with the stamped approval period will be sent/posted with the final approval letter and the study may begin.

⇒ The study is **approved with specified, non-substantive revisions.** The Investigator will receive a letter clearly indicating the required modifications. Upon receipt of the changed documents, the Committee Chairperson will verify that the appropriate additions/corrections were made and will approve the study. A final approval letter will be sent to the Investigator including the consent documents stamped with the corresponding approval period. If requested changes are substantive, the reviewers may choose to defer the study to the board.
⇒ **Study Deferred to Full Board**—The IRB Chairperson or designed expedited reviewers may refer the study to the Committee. If the application is referred for Committee review, the Investigator will be notified by the IRB. Whenever possible, the proposal will be included on the agenda for the next regularly scheduled Committee meeting. The reviewers may also request additional information, to be included for Committee review and, when appropriate, may request that the Investigator be present at the meeting.

**Full Committee Review**

A submitted study meeting these criteria is reviewed by IRB members, including primary reviewers with an appropriate area of expertise prior to the convened meeting. IRB members must have sufficient time to review the studies; therefore, a submission deadline is strictly enforced. Check the IRB website for meeting and deadline dates.

The following documents are necessary for full review:

⇒ A complete “new protocol submission xForm” or, for VA studies, the “VA new protocol submission xForm.”

⇒ The xForm must include the appropriate signatures.

Attachments must include:

⇒ All proposed Informed Consent Documents using the template available on the IRB website with version date as footer or header, if applicable

⇒ Complete protocol, when applicable

⇒ Any recruitment materials, including any advertisements intended to be seen or heard by potential participants

⇒ Any questionnaires, surveys, testing forms and/or introduction letters associated with the study and intended for participant use or view

⇒ Unaffiliated Investigator Form, if applicable

⇒ HIPPA Authorization to Use and Disclose Information Form, if applicable

⇒ A copy of the grant application, if applicable

⇒ CV of PI

⇒ If study has an associated contract, a copy of the contract, or at minimum, a copy of any contract pages referencing provisions for medical care or other care and services for research-related injury

⇒ Full protocol (if applicable)

⇒ Any relevant grant application (Investigators who are seeking funding, whether federal or otherwise, must submit a copy of the funding packet for review)
⇒ Investigator’s brochure, if there is one (investigational drugs only per 21 CFR 312)

⇒ For HHS supported multicenter clinical trials, a copy of the HHS approved sample informed consent document

⇒ For HHS supported multicenter clinical trials, a copy of the complete HHS approved protocol

⇒ If study has an associated contract, a copy of the contract, or at minimum, a copy of any contract pages referencing provisions for medical care or other care and services for research-related injury

⇒ If the PI is a student, the xForm must include a completed Faculty Assurance Statement.

**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 are 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 reviewers should conduct an in-depth review of all pertinent documentation. Reviewers may contact the investigator for clarification or additional information.

**Convened Meetings**

Applications for consideration at the convened meeting of the IRB are made available to the Primary Reviewers and the members of the IRB prior to the convened meeting. 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. 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. Initial full reviews will be individually presented, and discussed by the IRB as a whole group. In conducting the initial review of proposed research, the IRB reviews information in sufficient detail to make the determinations required under DHHS Regulations at 45 CFR46.111. Approval will only be granted after substantive review and careful consideration of the determinations required under HHS Regulations at 45 CFR46.111.
**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 or 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 on the application, 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 adversely on the risk/benefit ratio or to supply missing materials.

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.

**Results of Full Committee Review**
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

**Approvals:**
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. (Refer to continuing review policy)

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. 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.

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 involving risks to participants or others 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.

An approved copy of the Informed Consent document will also be sent/posted. 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. 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. A stamped, dated and initialed copy of the approved Informed Consent, mirroring the last approved ICD forwarded to the investigator, will be maintained in the OPHRS located on the campus of East Tennessee State University.

Additionally, copies of all correspondence, including a copy of approved ICD, are cc’d to the VA Research & Development (VA R&D) office for all VA investigators.

**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.

**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. (See Appeal policy)

**Research at the VA**

The James H. Quillen Veterans Affairs Medical Center is governed by VHA, DHHS, ORO and FDA regulations protecting the rights, safety, and confidentiality of human subjects in research. The VA Research & Development Committee (VA R&D)
functions under the mandate of codes and articles such as, Title 38 in the Code of Federal Regulation and VHA Handbook 1200.5. Ethical precepts included in The Belmont Report, the Nuremberg Code, the Declaration of Helsinki and Good Clinical Practice also apply. An approved Federalwide Assurance for the ETSU/VA IRB is on file with the Department of Health and Human Services Office for Human Research Protection.

Completion of compliance course(s) in the ethical conduct of human subject research is required prior to submission. Compliance education is verified at the time of submission. Research proposals/protocols will not be accepted by the VA R&D Administration until credentialing has been verified and the Principal Investigator and members of the research team (e.g., co-sub-investigator, research coordinators, etc.) have completed the VA CITI course, or a similar course(s). Proof of course completion will be required.

**NOTE:** Investigators seeking to conduct research at the James H. Quillen Veterans Affairs Medical Center (VAMC)* must additionally seek approval from the VA R&D prior to initiating research activity. VA R&D approval is, however, contingent upon IRB approval. Should assistance be required, contact the VA R&D Administration. (Contact Information on last page)

*defined as research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time

Go to www.etsu.edu/irb for VA submission Guidelines.