INTRODUCTION

On behalf of East Tennessee State University, thank you for your willingness to serve as a member of the IRB. To provide background information on the IRB and the roles and responsibilities of its members, as well as to remind you of the serious nature of this responsibility, this handbook has been specifically designed for IRB members.

It is the policy of *East Tennessee State University (ETSU) and the James H. Quillen Veterans Affairs Medical Center (VAMC) at Mountain Home (Johnson City), Tennessee to comply with all applicable local, state, federal, and international Good Clinical Practice (GCP) regulations as adopted by FDA in the conduct of human subject research. Written procedures are required to document the management of assurances of compliance. In accordance with the Federal Policy on the Protection of Human Subjects (Department of Health and Human Services [DHHS] Title 45, Code of Federal Regulations (CFR), Part 46, Food and Drug Administration (FDA) Title 21 CFR Parts 50 and 56, 38 CFR 16), ETSU and the VAMC are jointly responsible for the protection of the rights and welfare of human subjects of research conducted by, or under the supervision of physicians, faculty, staff, or students. Also, national and international communities have adopted ethical principles to guide the use of human subjects in research. These are: The Belmont Report, the Nuremberg Code, and the Declaration of Helsinki. To conduct this responsibility effectively, the University maintains Institutional Review Boards (IRB) to review research protocols involving human subjects and to evaluate both risk and protection against risk for those subjects. It is the function of the IRBs to 1) determine and certify that all research projects conducted by ETSU or by the VAMC, or by physicians, faculty, staff, or students of either institution, or for any institution for whom these services are provided by contractual agreement, conform to the regulations and policies set forth by the DHHS, Office for Human Research Protection (OHRP), the FDA, and other federal entities regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist the investigator in complying with federal and state regulations.

*Two Boards have been constituted within the Human Research Protection Program (HRPP) at East Tennessee State University to operate within the regulatory requirements of 45 CFR46.107. These boards address the needs of both the ETSU research community and that of the James H. Quillen Veterans Affairs Medical Center (VAMC). Institutional responsibility is clarified and applicable throughout this document as follows:

Purpose of the IRB

The purpose of the IRB is to ensure that humans involved in research at these institutions are afforded protection as described in the revised version of the Belmont Report, the Declaration of Helsinki, the International Conference on Harmonisation (ICH) Guidelines as adopted by FDA, Good Clinical Practices (GCP), the Health

The IRB shall have three major functions:

1. Assure the protection of human subjects involved in research or related activities;

2. Assure that East Tennessee State University and the James H. Quillen Veteran Affairs Medical Center fulfill their contractual and federally mandated obligations relative to the protection of human subjects; and

3. Maintain the policies and procedures for the protection of human subjects which are, at a minimum, in accord with applicable regulations of funding and regulatory agencies.

The primary concern of the IRB is the protection of the rights and welfare of human subjects in research [21 CFR 56.111(a)(1)-(5)(b)]. Toward that end, the IRB addresses:

1. identification of the risk

2. evaluation of the risk (e.g., a determination of whether or not the risk/benefit ratio is acceptable/appropriate);

3. evaluation of procedures to minimize risk

4. evaluation of the informed consent process which must adequately explain the risks and

5. privacy and confidentiality issues. All research involving human subjects at ETSU and the VA Medical Center must be submitted to the appropriate IRB for review.

The Belmont Report of April 18, 1979 contains the principles upon which the HRPP is based. These principles are:

⇒ Respect

⇒ Beneficence

⇒ Justice

Authority

The policies governing the IRB are in accord with the Federal-wide Assurance (FWA) numbers indicated above and filed with the Federal Office for Human Research Protections (OHRP). No research that involves human subjects may be undertaken at East Tennessee State University or the James H. Quillen Veterans Affairs Medical
Center, or other non-affiliated site(s) using either IRB, without the prior approval of the IRB.

**ETSU**

All individuals engaged in research that is sponsored by East Tennessee State University, conducted by or under the direction of any faculty, staff, or student or agent of ETSU in connection with his or her institutional responsibilities; conducted by or under the direction of any employee or agent of ETSU using any property or facility of ETSU; on involves the use of ETSU's non–public information to identify or contact human research participants or prospective participants must obtain ETSU or ETSU/VA IRB approval before beginning any research activities.

The IRB must review all human subject research if one or more of the following apply:

⇒ The research is sponsored by ETSU

⇒ The research is conducted by or under the direction of any employee, faculty, staff, student, or agent of ETSU in connection with his or her institutional responsibilities

⇒ The research is conducted by or under the direction of any employee or agent of ETSU using any of ETSU's property or facilities

⇒ The research involves the use of non-public information maintained by ETSU to identify or contact prospective participants or participants

⇒ ETSU is the recipient of a direct federal award to conduct human subject research, even where all activities involving humans are carried out by a subcontractor or collaborator

⇒ ETSU or ETSU/VA IRB is the IRB of record by contract or MOU

Approval by the VA Research & Development (R&D) Committee is additionally required for VA research (defined as research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time).

Any signatory Institution may deny a research project approved by the IRB, including projects exempted by the IRB Chair. No office of any of the participating Institutions may approve a research activity that has been disapproved by the IRB. No members who are responsible for business development may serve as members on the IRB or carry out the day-to-day operations of the review process.
Summary Composition

The requirements for the composition of the IRB under the revised Common Rule vary slightly from the 1991 Common Rule. The composition of the ETSU and ETSU/VA IRB complies with both rules.

The membership of each IRB will be based on the Federal policy requirements as described in 45 CFR 46.107. Individuals from the Research and Sponsored Programs Office at ETSU or the Research Office at James H. Quillen VA Medical Center do not serve as voting members of either IRB. No members who are responsible for business development may serve as members on the IRB or carry out the day-to-day operations of the review process.

Under the 1991 Common Rule, IRB Committees are required to have a minimum of five members each, with varying backgrounds and expertise to provide thorough and complete review of research activities commonly conducted by the Institution(s). Among the voting members the following constituencies will be represented: men and women, behavioral and social scientists, and non-scientists. Each IRB includes at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in non-scientific areas. Non-scientific primary concerns are those unambiguously in non-scientific areas, meaning little or no scientific or medical training or experience. Nurses, pharmacists, and other biomedical health professionals are not considered to have primary concerns in non-scientific areas. Each IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. The IRB will be composed so that its membership does not lack diversity, including consideration of race, gender and cultural backgrounds, experience, expertise, and sensitivity to such issues as community attitudes, necessary to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

Under the 2018 Common Rule, the following requirements apply to the composition of the IRB:
Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB is required to be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB will include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners,
individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects. The IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

The IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. [§ .107]

**ETSU/VA IRB:** According to the terms of agreement between East Tennessee State University and the James H. Quillen VA Medical Center, the ETSU/VA IRB will have the following composition. There shall be six (6) representatives from ETSU faculty. There shall be no less than 3 VA representatives who are a minimum 1/8th full-time employee equivalent, with two of the three VAMC representatives being members of the medical staff. There shall be four (4) ETSU staff representatives. At least one VA representative must have scientific expertise. There shall be two (2) representatives from the local community. The ETSU/VA IRB Committee must include at least one (1) member whose primary interests are in a scientific area, one (1) member whose primary interests are in a non-scientific area, and one (1) member who is not affiliated with East Tennessee State University or the James H. Quillen VA Medical Center (i.e. not a family member or spouse of an employee and not an active alumnus). The non-scientist and non-affiliated member may be the same individual. The roster will include at least one member who represents the perspective of research participants, such as a former or current research participant.

IRB members will be appointed by both the President of East Tennessee State University and the Director of the Veterans Affairs Medical Center upon recommendation of the Provost/Vice President for Academic Affairs, the Vice President for Health Affairs and the Associate Chief of Staff for Research (VA). The letter of appointment shall be affirmed with the signature of both the President and the VAMC Director.

R&D administrative officials including, but not limited to ACOS and AO, are prohibited from serving as voting members of the IRB. The VA RCO may not serve as a voting or nonvoting member of the IRB. The VA RCO will be invited to attend all meetings of the ETSU/VA IRB and will serve as a nonvoting consultant to the ETSU/VA IRB. Individuals working on without compensation appointments or those with intergovernmental appointment act (IPA) appointments cannot be VA representatives. Facility Directors, their administrative staff, Chiefs of Staff, and other local leadership
may observe IRB meetings, but may not be voting or ex-officio, non-voting members of the ETSU/VA IRB.

**ETSU IRB:** The ETSU IRB members will be appointed by the President of East Tennessee State University upon recommendation of the Provost/Vice President for Academic Affairs, and/or the Vice President for Health Affairs. The letter of appointment shall be affirmed with the signature of the President. Per ETSU policy, the ETSU IRB will include at least nine voting faculty representatives as follows: one representative from the College of Business and Technology, one representative from the College of Clinical and Rehabilitative Health Sciences; one representative from the College of Nursing, one representative from the College of Public Health; one representing the humanities; one representing the social sciences within the College of Arts and Sciences; one representing the area of human development; one representing the areas of curriculum and instruction and educational leadership within the College of Education, and one representing the Faculty Senate. In addition, two ETSU Staff Representatives, two representatives from the local community, and one prisoner or prisoner representative with appropriate background and experience will serve as voting members. The prisoner representative must have a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner. Research involving prisoners as participants must be reviewed by the ETSU IRB. One voting member of the ETSU IRB must hold the M.D. degree.

The ETSU IRB Committee must include at least one member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area and one member who is not affiliated with East Tennessee State University (i.e. not a family member or spouse of an employee and not an active alumnus). The non-scientist and non-affiliated member may be the same individual. The roster will include at least one member who represents the perspective of research participants, such as a former or current research participant.

**Non-Voting Ex Officio Members**

The following are designated as non-voting ex officio or administrative members on both boards by virtue of their position or area of expertise: the Assistant to the President for Legal Affairs at ETSU, the IRB Director, IRB Coordinators, and IRB Information Research Technician. Their terms shall be indefinite.

On the ETSU/VA IRB, the Administrative Officer of the Quillen VA Medical Center Research and Development Office will be appointed as a non-voting ex officio member for an indefinite term. In addition, for the approved term of service, the Director of Pharmacy Services at Johnson City Medical Center Hospital shall also serve as a non-voting member of the ETSU/VA IRB. The ETSU Privacy Officer and a Mountain States Health Alliance representative will also serve as ex officio members of the ETSU/VA IRB.

Unless the Chair of the Quillen VA Medical Center Research and Development Committee (VA R&D) has been appointed by the President of East Tennessee State University and the VAMC Director to serve as a regular voting member on the ETSU/VA
IRB, the VA R & D Committee Chair will also be a non-voting *ex officio* member of the IRB. Their (*ex officio*) term shall run concurrently with the term of service on the VA R & D Committee.

*Ex officio* members, invited guests, and expert consultants do not have voting privileges. R&D administrative officials including, but not limited to ACOS and AO, are prohibited from serving as voting members of the IRB.

**Consultants**

If an IRB member with sufficient expertise adequate to the scope and complexity of the research proposal is not available, the Chair will ask a consultant with such expertise to review the study and provide written recommendations. Consultants may evaluate research for any issues requested by the IRB. A conflict of interest form must be completed by the consultant prior to review, and a consultant may not review research if any conflict of interest is identified. In addition, consultants must agree to confidentiality prior to review. Consultants may attend the IRB meeting but will not count toward quorum or vote.

**Community Members**

45 CFR 46.107 specifies that there must be representation on the IRB that is sensitive to issues such as community attitudes. The community member serves as a consumer representative and as the ethical conscience of the Board. Community members provide valuable insight in analyzing the Informed Consent Document (ICD) for clarity and understandability. They are invaluable in discussions of risks and benefits, and function as an effective link between the IRB, the investigator and the community. Their success reinforces and strengthens public trust in research. The community member provides the perspective of the individual or subject. The regulations at 38 CFR 16.107 require that the IRB have at least one member not otherwise affiliated with the VAMC. Community members must attest in writing that neither they, nor any family member, are affiliated with ETSU or (for the ETSU/VA IRB) the VA affiliate covered under these assurances (IRB Membership Certificate 101). The signed attestation will be maintained in the Office for the Protection of Human Research Subjects (OPHRS) membership records for a period of three years beyond the end of the term.

**Selection and Credentialing of IRB Membership**

The regulatory requirements regarding IRB membership as found in §46.107 apply. The IRB must have sufficient expertise and diversity to evaluate ethical issues involved in protocols presented for review and approval. Selection of potential IRB members is made based on recommendations from Committee members, Service Chiefs, Department Chairs, and Deans. Committee member selection must be made with the goal of maintaining appropriate IRB diversity, expertise, and regulatory compliance.

Acting upon recommendations received, at minimum, a curriculum vita or résumé must be submitted along with a written affirmation of, degrees, certificates earned, technical areas of expertise, etc. (form 101) for each IRB nominee. The IRB Chairs, Director, and
for ETSU/VA IRB, the VA AO will review all documents submitted to identify those nominees exhibiting technical expertise or other pertinent qualifications to review the types of research commonly presented to these Boards. Supporting documentation for appointment recommendation will be forwarded to the Vice Provost for Research (VPR) by the Director. The VPR will forward the final selection of nominees to the Provost/Vice President for Academic Affairs, the Vice President for Health Affairs, and (for ETSU/VA IRB) the Associate Chief of Staff for Research. Documents supporting final appointments to either Board, along with records of continuing education, will become a part of the permanent membership records maintained by OPHRS. The configuration of the IRB membership will be reviewed, at least annually by the institutions, including the VA Research and Development Committee. Substantive changes will be reported to OHRP and (for ETSU/VA IRB) to the VA AO by the OPHRS Director. The Medical Center Director is responsible for reporting changes in rosters to ORO Central Office with a simultaneous copy to the appropriate ORO Research Officer.

Consistent documentation of the following will be required from each member of the IRB at initial appointment and annually, and will be made available as appropriate, upon request, during conditions of audit:

⇒ Completed Membership Certificate (IRB Form 101)
⇒ Current curriculum vitae
⇒ Attendance at 60% (at minimum) of the regularly scheduled IRB meetings, or [the members] contact with the ETSU Office for the Protection of Human Research Subjects (OPHRS) to inform the staff of potential absence, and [the members] contact with the alternate member assigned to them in order to have the alternate attend in their stead
⇒ Participation in the required training and New Member Orientation within the first 30 days of appointment;
⇒ Documentation of current institutional certification (as appropriate) in compliance education in the conduct of human subject research (please refer to education policy)

In addition, the IRB maintains documentation of participation in continuing education opportunities made available throughout the year.

**Attendance:**

Attendance at the meetings of the IRB is crucial. To insure quorum, in the event the regular member cannot attend, it is the responsibility of the member to contact their appointed alternate member to attend in their stead. Notification of the change should additionally be forwarded to OPHRS. If a voting member has been unable to attend at least 60% of the meetings of the IRB during one year, and has not contacted their alternate member to attend in their stead (to guarantee quorum), the member will be relieved of their position on the IRB, through written notification, over the signatures of
the IRB Chair and the OPHRS Director. For ETSU/VA IRB members, the medical center director must additionally sign the written notification. A new voting member will be appointed to the vacant position, selected from the pool of alternates or identified through solicitation of the Department Chairs, Deans, or appropriate other.

For ETSU/VA IRB, the medical center director is responsible for suspending or terminating the IRB membership of any individuals who are not fulfilling their member responsibilities or obligations.

**Length of Appointment**

The term of appointment to the IRB for voting members and alternates shall be three (3) years. Members may be reappointed to additional terms at the discretion of the University President, and for the ETSU/VA IRB, the VA Director. VA representatives to the ETSU/VA IRB are appointed for a period of three years and may be re-appointed to a new three year term without lapse in service at the end of each term.

**Frequency of Meetings**

The medical IRB will meet monthly. The campus IRB will meet every month during the academic year, with one meeting during the summer, with additional meetings scheduled if issues or studies that require full board deliberation are received. Additional meetings may be called at the discretion of the Chair of the IRB.

**Chair and Vice Chair**

Both the Chair and the Vice Chair play a leadership role in establishing and implementing IRB policy. As primary representatives of IRB decisions, the IRB Chair shares authority over all IRB policy and procedures in collaboration with the Institutional Official and the Director. The Chair should be willing to represent the institutions in discussions with federal authorities, and should review all protocols presented to the full-committee. The Chair/Vice-Chair is encouraged to communicate with other reviewers so that important IRB issues are resolved or identified before the convened meeting. The Chair directs the proceedings and discussion of the convened meeting and is a voting member with full privileges except in instances of declared conflict of interest. Additionally, 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). These individuals should have an in-depth understanding of the ethical issues, state law, institutional policy, and federal research regulations applicable to the types of studies reviewed by the IRB.

The Chairs and Vice Chairs are credentialed and appointed as indicated above. In addition, they should have familiarity in conducting meetings of this type, interpersonal skills, leadership and a background and reputation that encourage respect from the IRB membership, the administration, and local researchers. Their profession should mirror the focus of the Board (recommended MD for the ETSU/VA IRB, PhD [social or behavioral scientist] for the ETSU IRB).
In the Chair’s absence, the Vice Chair will have signatory authority and shall act in all matters concerning the functions of the IRB.

In the absence of both the Chair and the Vice Chair, the IRB may appoint a temporary acting chair with the approval of the VPR for ETSU IRB and both the VPR and ACOS/R for ETSU/VA IRB. At the time of the scheduled meeting, the following criteria must exist for the acting chair: 1) served three or more years on the IRB, 2) current certification in human subject research compliance education.

**Compensation**

The Chairs will receive a small stipend in support of their efforts in the review of human subject research. Members of the IRB will not be compensated for their service on either Board.

**Liability**

The Institutions acknowledge that their respective employee and community members of the IRB are covered under the liability programs of the Institutions for their participation in the actions of the IRB.

**Conflict of Interest**

IRB members are considered to have a conflicting interest whenever any one of the following is true:

⇒ The IRB Committee Member, Consultant, IRB staff or a member of their immediate family has a significant financial interest as defined in Policy 17a.

⇒ The IRB Committee Member, Consultant, IRB staff or a member of their immediate family is a member of the research team designing, conducting, or reporting the research presented in the protocol, or has an immediate family members involved in the design, conducting or reporting the research presented in the protocol.

⇒ The IRB Committee Member, Consultant, IRB staff, or a member of their immediate family has any other interest of any kind that the individual believes conflicts with his or her ability to objectively review a protocol

At the beginning of each meeting, the IRB Chair calls for disclosure of conflicting interests on any agenda item. This includes, but is not limited to, initial reviews, continuing reviews, modifications, and reports of unanticipated problems. IRB Committee Members and IRB staff are responsible to declare any conflicting interest to the IRB before review of the protocol. An IRB Committee Member who declares a conflicting of interest may not participate in the review of research at a convened meeting except to provide information requested by the IRB. An IRB Committee Member who declares a conflict of interest must leave the room during discussion and voting.
IRB Committee Members who are absent from the meeting room for a conflicting interest are not counted towards quorum when the vote on the study in question is taken. The minutes will reflect that the IRB Committee Member was absent due to a conflicting interest.

An IRB Committee Member who declares a conflict of interest may not participate in the expedited review process of any involved study. He/she must indicate that conflict and notify the IRB Coordinator for re-assignment.

The above policy includes initial review, continuing review, review of modifications, review of unanticipated problems involving risks to participants or others, and review of non-compliance with the regulations or IRB requirements.

In addition, IRB staff must reveal any conflict of interest on any involved study, and alternate staff assignment as appropriate will be made by the Director.

IRB staff members are responsible to inform Consultants of this policy and identify any conflicting interest to the IRB before use of the Consultant. A conflict of interest form must be completed by the consultant prior to review, and a consultant may not review research if any conflict of interest is identified.

Confidentiality

The IRB membership must be diligent to maintain confidentiality. The Board must be free to deliberate in private without fear of coercion. With the exception of the IRB Chair or Vice-Chair, at no time may a member discuss deliberation content or outcomes with investigators post-review. The IRB policy is to notify the investigator in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. The OPHRS staff will be responsible for dispatching written notifications (post-deliberation), to the appropriate investigator.

Designated IRB members tasked with conducting primary reviews of initial submissions, continuing reviews, or reviews of unanticipated events are authorized by the convened board to contact the Principal Investigator to discuss issues related to clarity, risk, benefits, etc.

Designated IRB members tasked with conducting primary reviews of initial submissions, continuing reviews, or reviews of unanticipated events are authorized by the convened board to contact the Principal investigator to discuss issues related to clarity, risk, benefits, etc.

Quorum

A quorum will consist of a majority (more than 1/2) of the voting members of the IRB, including one member whose primary concerns are in the non-scientific area, as is required by 45 CFR 46.108.
For the ETSU/VA IRB, at least one voting VA representative must be present for VA research to be considered. If research involving an FDA-regulated article is being reviewed, a licensed physician must be included in the quorum.

In order for research to be approved, it must receive the approval of a majority of those members present at the meeting. If at any time during the meeting the quorum fails, further votes cannot be taken unless the quorum is restored. The recording of the vote will denote the number of votes for, opposed and abstained. If the only non-scientist representative must leave the meeting for brief period, the IRB will take no further actions or votes until the non-scientist returns to the meeting.

If a quorum should fail during a meeting, (i.e., loss of majority through abstentions of members with conflicting interests, early departures, or absence of a non-scientific member), the IRB will not take any further actions unless a quorum can be restored.

When reviewing a protocol involving children, the IRB will ensure that appropriate pediatric expertise is available to review the specific research activities. Non-voting consultants may be invited to assist with the review if additional expertise is needed.

When reviewing a protocol in which a prisoner is a subject,

⇒ A majority of the IRB (exclusive of prisoner members or prisoner advocates) must have no association with the prisoner(s) involved, apart from their membership on the IRB;

⇒ At least one IRB member present at the meeting shall be a prisoner, or a prisoner advocate /representative with appropriate background and experience to serve in that capacity.

PRISONER/PRISONER REPRESENTATIVE MUST BE PRESENT AS VOTING MEMBER for the review of any studies (including initial review, continuing review, modification, or report of unanticipated problems involving risks to participants and others) that involve prisoners.

When reviewing research funded by the National Institute on Disability and Rehabilitation Research that purposely requires inclusion of children with disabilities or individual with mental disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these participants.

For VAMC research that involves mentally disabled persons or persons with impaired decision-making capacity, IRB membership must include at least one member who is an expert in the area of the research.

The requirements for the composition of the IRB under the revised Common Rule vary slightly from the 1991 Common Rule. The composition of the ETSU and ETSU/VA IRB complies with both rules.
Under the 1991 Common Rule, when reviewing studies with other vulnerable populations, including pregnant women, fetuses, neonates, handicapped persons, and cognitively impaired, the IRB will request review by expert consultant, as needed. If the IRB regularly reviews research involving a vulnerable category of subjects, one or more individuals who are knowledgeable about and experienced in working with these subjects should be included as IRB members (refer to policy on vulnerable subjects for more details).

Under the 2018 Common Rule, if the IRB regularly reviews a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration will be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

Board members are contacted per email approximately 7-10 days prior to the scheduled meeting date and asked to confirm their planned attendance to ensure appropriate notification of alternates. Meeting attendance is one of the most important services of committee members and alternates. It is critical that members and alternates notify OPHRS staff of their availability for meetings. A quorum worksheet is completed by the IRB Coordinator, Director, or Chair to determine and document whether the IRB meeting is appropriately convened.

Alternates

It is very important that members attend every possible meeting. The IRB does have a pool of alternates that are designated to replace regular members at meetings that the regular members cannot attend. The alternates are selected so that their expertise matches that of the regular voting members. This ensures that the federal requirements for an IRB are met if an alternate is serving in place of a regular member. Alternates are selected for the IRB upon approval of the Provost/Vice President for Academic Affairs and the Vice-President for Health Affairs, and (for the ETSU/VA IRB) the Director of the James H. Quillen Veterans Affairs Medical Center.

Members who cannot attend a meeting must contact the ETSU Office for the Protection of Human Research Subjects (OPHRS) to inform the staff of potential absence. It is the responsibility of the member to contact their appointed alternate member to attend in their stead. If a voting member has been unable to attend at least 60% of the meetings of the IRB during one year, and has not contacted their alternate member to attend in their stead (to guarantee quorum), the member will be relieved of their position on the IRB, through written notification, over the signatures of the IRB Chair and the OPHRS Director (and for ETSU/VA IRB, the MCD). A new voting member will be appointed to the vacant position, selected from the pool of alternates or identified through solicitation of the Department Chairs, Deans, or appropriate other.

Alternate members have full voting authority only in the absence of the regular member. If you are serving as an alternate, your length of service will be the same as the term of the voting member. Although the function of an alternate member is to replace a
regular member who cannot attend a meeting, alternates should rotate their attendance at meetings, so as to gain from their experience in serving on the IRB. The IRB meeting minutes document when an alternate member replaces a voting member.

Alternates may be recommended by the Chair, for election to vacant, un-expired terms and three year terms for which they qualify on the regular committee.

Training

There are various mechanisms by which new members receive training and become oriented to the Committee’s functions, policies, and procedures. New members are invited to an orientation with the IRB staff and/or IRB Chairs and given a packet of pertinent information. This information is also available on the IRB website.

New IRB members are required to complete the same training required of investigators at ETSU within 30 days of appointment.

Review of the IRB

The Office for the Protection of Human Research Subjects (OPHRS) will be audited by the East Tennessee State University Department of Internal Audit, at least once every five years. This department’s function is guided by the Institute of Internal Auditor’s Statement of Responsibilities, Code of Conduct, and the Standards for the Professional Practice of Internal Auditing. The audit includes evaluation of the adequacy of internal controls, and the level of compliance with institutional policies in addition to government laws and regulations.

The audit report will be forwarded as follows:

⇒ Tennessee State Audit Office (ETSU),
⇒ Office of the President,
⇒ Provost for Academic Affairs,
⇒ Vice Provost for Research, VP for Health Affairs,
⇒ Director (OPHRS),
⇒ VAMC Office of the Director,
⇒ Associate Chief of Staff for Research,
⇒ VHA Office of Research Oversight (ORO),
⇒ VISN 9

The OPHRS is additionally audited by external entities, which may include but are not limited to, the Food and Drug Administration (FDA), Office for Human Research
Protection (OHRP), ORO, Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP), and Mountain States Health Alliance Corporate Compliance and Auditing Services. When these audits occur, a copy of the audit outcome, along with associated responses will be forwarded to the ETSU Office of Internal Audit.

The IRB membership and composition is reviewed on an annual basis by the ETSU Office of Internal Audit. In addition, the VA Research and Development Committee review the membership and composition of the ETSU/VA IRB on an annual basis. Findings and any recommended adjustments are forwarded to the IRB Chair, Director, and the Vice Provost for Research.

Meeting Agendas

At each meeting, the Chair or Vice-Chair will lead the discussion following the agenda provided in IRBManager. The Chair will also inform the committee of any changes or issues that have come up in the course of the month.

Meeting Notifications

Approximately 10 days prior to each meeting, the IRB members are notified of the upcoming meeting. At that time, the agenda and required items for review are viewable in IRBManager.

IRB Committee Responsibilities

The IRB is responsible for reviewing research projects involving human subjects proposed by students at, or employees of, East Tennessee State University and employees or medical staff of the James H. Quillen Veterans Affairs Medical Center and for any institution for whom these services are provided by contractual agreement. Activities must meet the definition of “research” and involve “human subjects” as defined in DHHS regulations, or be “research” and involve “human subjects” as defined in FDA regulations to be subject to the IRB’s jurisdiction. See the IRB website for both DHHS and FDA regulatory definitions.

Committee members must:

1. Have an understanding of the basic ethical principles, regulatory requirements, and IRB policy and procedures.

2. Conduct all review, including prospective and continuing review, according to all applicable regulations, including DHHS regulations at 45 CFR 46; FDA regulations at 21 CFR 50 and 56; federal, state, and local laws; institutional policies and procedures; and when applicable, VA regulations including 38 CFR 16.

3. Evaluate research for both scientific and scholarly merit (refer to scientific review policy)
4. Identify any conflict of interests prior to review of research (refer to conflict of interest policy)

5. Obtain guidance/expertise as needed to conduct a complete review

Institutional Review Board responsibilities include:

1. Assures compliance with the FWA

2. Assures ETSU policies and procedures are effectively applied in compliance with State and Federal laws and regulations, the FWA, OHRP, FDA, NIH, OCR, and any other applicable federal agencies (including ORO for ETSU/VA IRB)

3. Provides interpretation and application of federal regulations

4. Develops, implements, and interprets IRB policies and procedures.

5. Takes action on non-compliance according to the IRB policies and procedures, if necessary

6. Supports and facilitates the IRB process.

7. Participates in mandatory training as well as other ongoing educational activities to keep abreast of current events.

Approvals of Research

The duties and responsibilities of the members of the IRB are best described by reproducing the statement published in 45 CFR 46.111.

The IRB will review and has authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.

§46.111 Criteria for IRB approval of research.

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

For research subject to the 1991 Common Rule and FDA research:

(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.

*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.

For non-FDA research subject to the 2018 Common Rule:

The IRB will review and has authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy. For studies subject to the 2018 Common Rule, this will include exempt research activities under §__.104 for which limited IRB review is a condition of exemption (under §__.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8)).

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 that are consistent with sound research design and that 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. 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 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, 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

At the time of this policy revision, ETSU is not allowing exemption under exempt categories 7 and 8. However, the information regarding limited review is included below.
(8) For purposes of conducting the limited IRB review required by §__.104(d)(7)), the IRB need not make the determinations at paragraphs (a)(1) through (7) of this section, and will make the following determinations:

(i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of §__.116(a)(1)-(4), (a)(6), and (d);

(ii) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with §__.117; and

(iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, 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, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

**Considerations when reviewing**

When evaluating the research plan to determine whether adequate provisions exist to protect the privacy of participants, the IRB considerations include:

⇒ The participant’s expectation of privacy, including influence of age and cultural norms of the proposed population. For example, a very young child will want his parents present, but a teenager would be embarrassed to answer personal questions in front of his parents.

⇒ That the informed consent provides potential participants adequate information about what they may be asked and what they will experience. Consider whether the participants will think whether the information being obtained is any of the investigator’s business.

⇒ That the setting of the research provides adequate privacy for participants to be comfortable in the setting (for example, participants may be uncomfortable having physical measurements taken in a setting that is not private)

⇒ That recruitment methods protect privacy (for example, recruiting in waiting room prior to a sensitive or invasive procedure may not protect privacy)
⇒ The sensitivity of the research (in general, the more sensitive, the greater the need for more stringent provisions for privacy and confidentiality.

When evaluating the research plan to determine whether adequate provisions exist to protect the confidentiality of participants, the IRB considerations include:

⇒ The sensitivity of the information and the protections offered to the participants
⇒ Whether there is accurate information in the consent process about who will have access to the records and the precautions being taken to protect confidentiality
⇒ Proposed data security measures, for example, methods of coding, de-identification, encryption etc.
⇒ Security of proposed storage/transfer plan
⇒ Whether access restrictions are appropriate
⇒ Whether broader categories of data collection should be used to prevent deductive identification (for example, age range rather than birthdate)

When evaluating the provisions for monitoring data to ensure the safety of participants, IRB considerations include:

⇒ What safety information will be collected, including serious adverse events
⇒ How the safety information will be collected (e.g. with case report forms, at study visits, by telephone calls with participants
⇒ The frequency of data collection, including when safety data collection starts
⇒ The frequency or periodicity of review of cumulative safety data
⇒ If study has a data safety monitoring committee and plan for reporting the data monitoring committee findings to the IRB and sponsor
⇒ For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB or EC needs to carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.
⇒ If not using a data monitoring committee, and if applicable, statistical tests for analyzing the safety data to determine whether harm is occurring;
⇒ Provisions for the oversight of safety data (e.g., by a data monitoring committee).
⇒ Conditions that trigger an immediate suspension of the research, if applicable.
When reviewing the assessment about whether the selection of participants is equitable, IRB considerations include:

⇒ The purposes of the research
⇒ The setting in which the research will be conducted
⇒ Whether prospective participants will be vulnerable to coercion or undue influence
⇒ The selection (inclusion/exclusion) criteria
⇒ Participant recruitment and enrollment procedures
⇒ The influence of payments to participants

**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 either 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. Each reviewer is responsible for reviewing all of the following study related documents, which will be viewable approximately 10 days prior to the meeting:

a. A complete IRB application with signatures. If the PI is a student, the Chair or Committee Chair must be named as a co-investigator on the application. The new protocol submission xForm includes a narrative portion and conflict of interest portion, in addition to additional sections.

b. All proposed Informed Consent Documents using the template available on the IRB website with version date as footer or header

c. Complete protocol, when applicable

d. Any recruitment materials, including any final ad(s) intended for participant view or use.
e. Copy of all research related measures (questionnaires, surveys, tests, interview question outline, including email solicitations, etc.)

f. For HHS supported trials, a copy of the HHS-approved sample ICD

g. For HHS supported trials, a copy of the complete HHS approved protocol if applicable.

h. Investigator’s brochure, when applicable

i. Unaffiliated Investigator Form, if applicable

j. HIPPA Use and Disclose Information Form, if applicable

k. A copy of the grant application, if applicable

l. Investigator CV

m. For student studies, a completed Faculty Assurance Statement in the xForm

n. Any consultant’s report, if available at the time of packet distribution.

o. If the study has a 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

The Primary IC 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 Reviewer Evaluation Form for Full Initial Reviews (xForm 111) to provide documentation of consideration of required elements for study approval. The Primary IC reviewer additionally completes Informed Consent Requirement Form (xForm section 128).

**Initial Full Review Approvals**

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 45 CFR 46.111. IRB members receive the materials sufficiently in advance of the meeting date to allow review of the material.
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 new protocol submission xForm, 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.

IRB Committee Determinations

After review, the possible actions which may be taken by the IRB are:

⇒ **Approval of the proposal**: An approval is granted if the research activity meets the criteria for approval as defined in 45 CFR 46.111 (see page 17) and no changes are recommended to the proposal.

⇒ **Approval with stipulations**: An approved pending status is given if the research meets the 45 CFR 46.111 criteria for research approval and any modifications required by the IRB require simple concurrence by the Investigator. When the modifications requiring simple concurrence are received from the investigator, the Chair or his/her designee may then review and confirm the modifications through an expedited procedure. The proposal may be referred back to the full committee if deemed necessary by the Chair or his/her designee.

⇒ **Defer pending receipt of additional information**: When the convened board requests substantive modifications or clarifications directly relevant to the determinations required 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.

⇒ **Disapproval**: Disapproval is given if the proposal does not meet the criteria for approval as defined in 45 CFR 46.111 (refer to page 17). If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

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 following criteria are considered when determining the review interval for full studies:
In determining which studies require review more often than annually, the IRB will consider:

(A) The nature of and any risks posed by the clinical investigation.
(B) The degree of uncertainty regarding the risks involved.
(C) The vulnerability of the participants.
(D) The experience of the clinical investigator in conducting clinical research.
(E) The IRB’s previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).
(F) The projected rate of enrollment.
(G) Whether the study involve novel therapies
(H) other reasons as determined by IRB

Coercion

Any IRB member or staff who believes that they have been subject to inappropriate influence should report this immediately to the IRB Chair or the Director of the Human Subjects Research Protection Program, who will report the attempt to influence to the Vice Provost for Research and Sponsored programs. The Vice Provost for Research and Sponsored Programs will investigate, or have investigated, the attempt to influence and determine an appropriate response to the attempt based on penalties similar to those outlined in the University’s Scientific and Scholarly Misconduct Policy. This policy may be found on the University’s Research Ethics webpage

http://www.etsu.edu/research/researchethics.htm.

The Chair, Vice Chairs, and members of the ETSU/VA IRB have direct access to the Medical Center Director for appeal if they experience undue influence or if they have concerns about the ETSU/VA IRB.