Chapter 1 – Purpose and History of the Institutional Review Board

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. 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. ETSU applies the same policies and procedures for protections for participants in non-DHHS funded research.

*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:

**Participants**

One Institutional Review Board (IRB) serves the academic campus of ETSU and is designated as the East Tennessee State University Campus IRB (ETSU IRB). Its members primarily hold terminal degrees such as the Ph.D. or Ed.D. degree and are drawn from the Colleges other than the Quillen College of Medicine. 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. Staff and community representatives and one M.D. are included in its membership. The expertise is primarily in the social and behavioral sciences and in educational research. The ETSU IRB reviews non-medical research conducted by, or under the supervision of faculty, staff, or students of the institution. ETSU is responsible for the protection of the rights and welfare of human subjects engaged in the research activities reviewed for approval by this IRB. The participating

institutions in the second Board, designated as the Medical Campus ETSU/VA IRB, are East Tennessee State University and the James H. Quillen Veterans Affairs Medical Center. The second IRB serves the Quillen College of Medicine, the James H. Quillen VA Medical Center, and is also the IRB of record for Mountain States Health Alliance, a local hospital group. Its members are largely drawn from the Quillen College of Medicine and the James H. Quillen VAMC and hold either the M.D. or other doctoral degrees. Community members are included. Its expertise is in the medical sciences and clinical research. The Medical Campus East Tennessee State University/James H. Quillen Veterans Affairs Medical Center IRB (ETSU/VA IRB) reviews medical research conducted by, or under the supervision of physicians, faculty, staff, or students of either/both institutions. Research protocols submitted under contractual agreements from physicians and/or staff employed by any Mountain States Health Alliance (MSHA) institution are additionally reviewed for approval by the ETSU/VA IRB. East Tennessee State University (ETSU) and the James H. Quillen Veterans Affairs Medical Center (VA) at Mountain Home (Johnson City), Tennessee, are jointly responsible for the protection of the rights and welfare of human subjects engaged in the research activities reviewed for approval by this IRB. The rosters of both boards will include at least one member who represents the perspective of research participants, such as a former or current research participant.

The Institutional Review Board Administration, located on the campus of East Tennessee State University, serves as the official Human Research Protections Program (HRPP) provider for the James H. Quillen Veterans Affairs Medical Center. The HRPP is officially outlined and documented in the Policies and Procedures, the Memorandum of Understanding (MOU), and the OHRP approved Federal-wide Assurance. All policies are reviewed by both institutions and updated as necessary by the IRB.

Whether a study is reviewed by one board or the other depends upon the type of research, not just the College in which the investigators hold an appointment. For example, a study in exercise physiology would be reviewed by the Medical IRB if it involved evaluation of the effects of natural product ingestion on performance. The Chair of either IRB may request that a study scheduled for review by their IRB be transferred to the other IRB if the other IRB may be the more appropriate one for review. However, all VA research must be reviewed by the ETSU/VA IRB. Research involving prisoners must be reviewed by the ETSU IRB.

Except where explicitly separated in the following sections, these Policies and Procedures apply to both IRBs and all non-affiliated investigators and sites using either IRB (including those sites for which services are provided through contractual agreement). Additionally, sites where ETSU employees and students conduct research may, by agreement, use either IRB.

Purpose
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 Good Clinical Practices (GCP) as adopted by FDA, the Health Insurance Portability and Accountability Act of 1996 (HIPAA), all applicable Federal Regulations governing human subjects research, and the moral and ethical precepts of the Institutions.
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

Statements supporting these ethical principles and standards adopted by the ETSU IRB can be found in the “The Nuremberg Code”, “The Declaration of Helsinki” and “The Belmont Report”. The principles of the Belmont Report are addressed in the IRB training and on the IRB website (www.etsu.edu/irb) as a reference, and shall be applied to the review and conduct of all human subject research.

Federal Wide Assurance
The institutions function under assurances approved by the Federal Office for Human Research Protections (OHRP) under the Secretary, Department of Health and Human Services as:

East Tennessee State University    FWA#00002703
James H. Quillen Veteran Affairs Medical Center    FWA#00002117

The Institutional Review Boards (IRB), operating within these assurances, are registered and identified as:

East Tennessee State University Campus Institutional Review Board
(ETSU IRB)    Non-medical research    IRB #00000256

Medical Campus East Tennessee State University /James H. Quillen Veterans Affairs Institutional Review Board
(ETSU/VA IRB)    Medical research    IRB#00002054
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 any 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.

The IRB has the authority to initiate periodic compliance reviews and/or directed audits. When necessary to assure protections of humans in research, the IRB may appoint a designee to observe the informed consent process of IRB approved research.

When issues of noncompliance or situations in which a participant in a research project has been exposed to unexpected serious harm are identified through an audit or compliance review, the IRB will promptly address such findings to assure that all research is being conducted in accord with the Federal-wide Assurance (FWA) numbers.
conducted according to Federal regulations, institutional policies and IRB policies and procedures.

The IRB has the authority and responsibility to suspend or terminate approval of research that is not being conducted in accordance with the policies and procedures of the institution or that has been associated with unexpected harm to participants or others. Any letter of suspension or termination of approval to an Investigator must include a statement of the reasons for the action by the IRB.

**IRB Jurisdiction**
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.

**Definitions:**

**Research** is defined in the DHHS Federal regulations (45 CFR 46) as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” Research is defined in the FDA federal regulations as any experiment that involves a test article and one or more human participants and that either is subject to requirements for prior submission to the Food and Drug Administration under Section 505(i), 507(d) or 520 (g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. Under FDA regulations the terms “research” and clinical investigation are synonymous. VA Handbook 1200.5 defines research as “the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data and interpreting the results in terms of the hypothesis or question. 38 CFR 16.102 states that “Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”

**Human Subjects** are defined in the “Common Rule” as “living individuals about whom an investigator (whether professional or student) conducting research obtains either (1) data through intervention or interaction with the individual or (2) identifiable private information.” FDA regulations define subjects as an individual who is or becomes a participant in research, either as a recipient of the test article or control. Subjects may be either a patient or a healthy human. FDA regulations also define subjects as an individual upon whose specimen a device is used. 38 CFR 16.102 defines a human subject as meaning “a living individual about whom an investigator (whether professional or student) conducting research obtains 1) Data through intervention or interaction with the individual, or (2) Identifiable private information.

**Systematic Investigation** means typically a predetermined method for studying a specific topic, testing a specific hypothesis(es), answering a specific question or developing theory.
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Generalizable—to develop or contribute to generalizable knowledge typically means that results or conclusions of the activity are intended to be extended beyond a single person or an internal program.

Intervention is defined as including both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant’s environment that are performed for research purposes. 38 CFR 16.102(f) notes that “an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.”

Interaction includes communication or interpersonal contact between investigator and participant.

Test article is defined as any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

Private Information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Investigational New Drug (IND) means “a new drug, antibiotic drug, or biological drug that is used in a clinical investigation”

Determining Whether a Proposed Activity is Human Research According to DHHS or FDA Regulatory Definitions

Activities that constitute human subject research are determined by the ETSU and ETSU/VA IRB. The IRBs delegate this decision to the IRB Chair or Vice Chair. The Chair or Vice Chair determines whether a proposal submitted to the IRB is human research according to DHHS or FDA regulatory definitions. If a protocol submitted to the IRB is determined to not be human research according to DHHS or FDA regulatory definitions, the submitter is notified in writing that the proposed activity does not fall under IRB jurisdiction. If the activity meets the FDA definition of “research” and “human subjects” as defined in FDA regulations, the IRB will adhere to all applicable FDA regulations. For drugs, the FDA regulations apply where there is any use of a drug in research except the use of a marketed drug in clinical practice. For devices, FDA regulations apply to studies where the purpose is to determine the safety or effectiveness of a device or data will be submitted to or held for inspection by FDA as part of a marketing permit. Note that when medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines unidentified tissue specimens as human subjects.

The IRB has the sole authority to make a final determination of whether a proposed activity is human research according to DHHS or FDA regulatory definitions. Unless you are familiar enough with these regulations to be certain that the activity does not represent human research, the activity should be brought forward to the IRB for a determination. A form 129
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(available at the IRB website) requesting a determination of whether the proposed activity is human research must be completed and submitted to the IRB office prior to beginning the project. The IRB Chair will review the form 129 and determine whether the proposed activity meets the definition of human research. The Chair or Vice Chair may not make this determination if he/she has direct involvement in the activity being examined. A written response will be returned to the submitter.

**Oral History**

Oral History is a method of gathering and preserving historical information through recorded interviews with participants in past events and ways of life. Most oral history interviewing projects are not subject to the requirements of the regulations found at 45 CFR 46.102(d) which define research as, “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge”. While historians reach for meaning that goes beyond the specific subject of their inquiry, unlike researchers in the biomedical and behavioral sciences, they do not reach for generalizable principles or laws of nature that have predictive value and can be applied to other circumstances for the purpose of controlling outcomes.

For these reasons, oral history interviewing in general, does not meet the regulatory definition of research as articulated in 45 CFR 46. Office for Human Research Protections (OHRP) concurs with this policy, as evidenced by the OHRP draft statement, dated 8/26/03. However, the IRB has the sole authority to make a final determination of whether a proposed activity is human research according to DHHS or FDA regulatory definitions. Unless you are familiar enough with these regulations to be certain that the activity does not represent human research, the activity should be brought forward to the IRB for a determination.
### Other Activities

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<tr>
<th>Activity</th>
<th>Description</th>
<th>Approval Status</th>
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<tr>
<td><strong>Case Studies</strong></td>
<td>A single subject study with clear intent, before recruiting or interacting with the participant, to use data that would not ordinarily be collected in the course of daily life. The intent is to report and publish the case study.</td>
<td>YES</td>
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<tr>
<td><strong>Case Studies</strong></td>
<td>Retrospective review of a patient’s medical record with the intent to report and/or publish the summary.</td>
<td>Retrospective review of a single patient’s medical record with the intent to report and/or publish the summary AND only clinically indicated interventions or data collection were performed AND data is de-identified = NO. Exception: If any aspect of the case is unusual enough that the patient might be identifiable even though normal patient identifiers are removed, then it should be submitted. &quot; For case reports involving more than one patient, IRB should be consulted (by submitting a Form 129) to determine whether the case report is research. If the proposed case report activity involves 4 or more patients, it must be submitted as human subject research.</td>
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<tr>
<td><strong>Thesis or Dissertation Project</strong></td>
<td>Retrospective review of a patient’s medical records for use in an educational setting. The data will be de-identified.</td>
<td>NO</td>
</tr>
<tr>
<td><strong>Thesis or Dissertation Project</strong></td>
<td>Thesis or dissertation projects conducted to meet the requirements of a graduate degree are usually considered generalizable</td>
<td>YES, IRB review and approval required for thesis or dissertation projects that involve human subjects.</td>
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<tr>
<td><strong>Classroom projects</strong></td>
<td>Classroom activities designed solely for educational purposes</td>
<td>If the data will not contribute to generalizable knowledge, will not be published outside the classroom, will not result in an article, master’s thesis, doctoral dissertation, poster session, will not result in abstraction or result in any other publication or presentation = NO. If the data will result in any of these = YES.</td>
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All Research Involving Humans Must Be Reviewed by the IRB

The implications of engaging in activities that qualify as research subject to IRB review without obtaining such review are significant. It is against University policy to use such data to satisfy thesis or dissertation requirements.

Investigators who request approval to continue research that was not previously reviewed or to use data that was collected without IRB approval face the possibility that the IRB deny the application, as the IRB cannot give post-hoc approval.

The IRB may not approve applications where the Investigator has attempted to circumvent IRB policies and procedures regarding human research by collecting data as non-research and then applying to use them as existing data. It is therefore in the Investigator’s best interest to consider carefully the likelihood that he or she will want to use the data for research purposes in the future, and to err on the side of inclusion and seek IRB approval prior to commencing the work.

Oversight of Others Assisting in Research

An Investigator may delegate study related activities but he or she is ultimately responsible for the conduct of the study. It is the responsibility of each Investigator to assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of Tennessee and the policies of ETSU.

Every member of the research team is responsible for protecting participants in research. Sub-Investigators, study coordinators, nurses, research assistants, and all other research staff have a strict obligation to comply with all IRB determinations and procedures, adhere rigorously to all protocol requirements, inform Investigators of all serious and unexpected adverse reactions or unanticipated problems involving risk to participants or others, oversee the adequacy of the informed consent process, and take whatever measures are necessary to protect the safety, rights and welfare of participants.

Regardless of involvement in research, each member of the research community is responsible for notifying the IRB promptly of any noncompliance with applicable regulatory requirements or determinations of the designated IRB of which they become aware, whether or not they are directly involved in the research.

Engagement

An institution becomes "engaged" in human subjects research when its employees or agents

i. intervene or interact with living individuals for research purposes; or

ii. obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)].

The institution is automatically considered to be "engaged" in human subjects research whenever it receives a direct HHS award to support such research. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.
<table>
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<th>Performance Site Category</th>
<th>Description</th>
<th>FWA required?</th>
<th>Required approval</th>
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<tbody>
<tr>
<td>Category 1</td>
<td>engaged in research with federal research support or direct award for study</td>
<td>Yes</td>
<td>Submit copy of site IRB approval or request that ETSU IRB be IRB of Record.</td>
</tr>
<tr>
<td>Category 2</td>
<td>engaged in research with no federal research support or direct award for study</td>
<td>No</td>
<td>Submit copy of site IRB approval or request that ETSU IRB be IRB of Record.</td>
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<tr>
<td>Category 3</td>
<td>Performance site not engaged in research with established IRB</td>
<td>No</td>
<td>Submit copy of site IRB approval or request that ETSU IRB be IRB of Record.</td>
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<tr>
<td>Category 4</td>
<td>Performance site not engaged in research without established IRB</td>
<td>No</td>
<td>Submit letter of permission from the appropriate institutional official stating that the research may be conducted at site.</td>
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For a VA multi-site study, not only the principal Researcher, but also all local site Researchers, must obtain written approvals from the relevant local VA facilities’ IRBs of record and all other local committees, subcommittees, and other approvals according to the respective applicable local, VA and other federal requirements. Research cannot be initiated at any given site until the local Researcher has obtained written notification that the research can be initiated from the local associate chief of staff for research and development.