



IRB MEMBER'S HANDBOOK

ETSU Campus Board



ETSU/VA Board



East Tennessee State University Institutional Review Board
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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 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 CFR 46.107. 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, Good Clinical Practices (GCP), 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:

- ⇒ Assure the protection of human subjects involved in research or related activities;
- ⇒ 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
- ⇒ 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; or 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 research conducted at VA facilities or using VA patients, time or equipment.

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.

Summary Composition

The membership of each IRB will be based on the Federal policy requirements as described in 45 CFR 46.107. 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. 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.

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 three (3) representatives who are faculty at ETSU but have greater than half-time appointments at the James H. Quillen VA Medical Center (VAMC). There shall be four (4) ETSU staff representatives in addition to two (2) staff representatives that have appointments at the VAMC. At least one VA representative must have scientific expertise. There shall be two (2) representatives from the local community. There shall be one (1) representative from a Veterans Affairs service organization. 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.

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.

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.

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 Secretary. 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-Addendum 101a). 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 availability, 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,

Affairs, 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 VA AO is responsible for reporting IRB roster information to the VA Office of Research Oversight (ORO).

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.

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.

Frequency of Meetings

The IRB will meet monthly. 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, 3) served three or more years on an IRB reviewing subcommittee (e.g., primary reviewer, expedited reviewer, adverse event reviewer).

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 are 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 return the packet to 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), over the signature of the Chair, 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 a quorum. 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 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 detail).

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 can not 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 can not 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. 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, with concurrence of the regular membership, 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 and TBR policies in addition to government laws and regulations.

The audit report will be forwarded as follows:

- ⇒ Tennessee Board of Regents,
- ⇒ 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 each packet. The Chair will also inform the committee of any changes or issues that have come up in the course of the month.

Meeting Packets

Approximately 10 days prior to each meeting, the IRB members are sent a packet, which contains agendas for the meeting as well as all documents specified in the policies.

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 ETCU/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

§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:
 - ⇒ 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.

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.
- ⇒ 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.
- ⇒ 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](#).
- ⇒ Informed consent will be appropriately documented, in accordance with, and to the extent required by [§46.117](#).
- ⇒ When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.*
- ⇒ 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.

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 receives a copy of all of the following study related documents approximately 10 days prior to the meeting:

- a. A complete IRB application (Form 103) with original signatures. (form 103 available on the IRB website). If the PI is a student, the Chair or Committee Chair must be named as a co-investigator on the application.
- b. Narrative completed per guidelines
- c. All proposed Informed Consent Documents using the template available on the IRB website with version date as footer or header
- d. Complete protocol, when applicable
- e. Any recruitment materials, including any final ad(s) intended for participant view or use.
- f. Copy of all research related measures (questionnaires, surveys, tests, interview question outline, including email solicitations, etc)
- g. For HHS supported trials, a copy of the HHS-approved sample ICD
- h. For HHS supported trials, a copy of the complete HHS approved protocol
- i. Investigator's brochure
- j. Conflict of Interest form
- k. Unaffiliated Investigator Form, if applicable
- l. HIPPA Use and Disclose Information Form, if applicable
- m. A copy of the grant application, if applicable
- n. Investigator CV
- o. For student studies, a completed Faculty Assurance Statement
- p. Any consultant's report, if available at the time of packet distribution.
- q. [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 receives 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 (Form 111) to provide documentation of consideration of required elements for study approval. The Primary IC reviewer completes Informed Consent Requirement Form (Form 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 45CFR 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 Form 103, 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
 - ⇒ Approval with stipulations
 - ⇒ Defer pending receipt of additional information
 - ⇒ Disapproval
- a. **Approved:** 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.
 - d. **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.
 - c. **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.

- d. **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:

- Recommendations by another committee, such as the VA Research and Development Committee
- Consent being given by legally authorized representatives
- Identified conflict of interest of involved study personnel
- Research for which participants would be exposed to additional risk (i.e., disproportionate number or severity of unanticipated problems, Phase I study)

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>.

Informed Consent Process

Informed Consent is the knowing consent of an individual or his/her legally authorized representative which is obtained without undue inducement or element of force, fraud, deceit, duress, or other forms of constraint or coercion. Informed consent is not just a form or signature, but a process of information exchange that includes:

- ⇒ subject recruitment materials
- ⇒ verbal instructions
- ⇒ written materials
- ⇒ questions/answer session
- ⇒ agreement documented by signature

The investigator must obtain legally effective written informed consent prior to enrolling a subject in a research project unless a specific exemption or waiver has been approved by the IRB, thereby waiving the requirement for informed consent or the requirement to obtain signed informed consent. Unless the IRB waives the requirement, informed consent must be documented by the use of a written consent form approved by the IRB, and signed by the subject or the subject's legally authorized representative. The IRB reviews all informed consent documents for adherence to Federal regulations regarding the required elements of informed consent and for assurance of the adequacy of the information contained in the informed consent. The IRB has the authority to observe or to have a third party observe the consent process and the research. (refer to the quality improvement policy).

Whenever the IRB requires documentation of informed consent, before a subject can participate in the research, the consent document must be signed and personally dated by the subject or by the subject's legally authorized representative, and by the person who conducted the informed consent discussion. During this period of prospective enrollment, the investigator (or qualified designee) must ascertain, either during the preliminary telephone interview (interest query), face-to-face encounter or by review of the medical history, the subject's ability to provide consent (HIPAA regulations regarding sharing/access to PHI apply). Before participation in the research, the subject or the subject's legally authorized representative must be given a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the research, the subject or the subject's legally authorized representative must be given a copy of the signed and dated consent form updates and a copy of any authorizations to PHI, or amendments to the written information originally provided.

Level

The informed consent document must be written using language that can be understood by someone reading at the seventh grade level. Medical terminology should be avoided or defined. The consent form is a statement addressed to the participant and should read as such. Separate forms may be required for different participant groups (parents, children) as well as for release of particular types of information (photographs, audio recordings video recordings).

Version Date

All Informed Consent Forms must bear a version date in the footer on each page of the consent. The version date must be updated whenever a revision is made to the informed consent document. (refer to modification policy)

Elements

The informed consent document must contain all the required elements of Informed Consent, as well as any pertinent additional elements

Required Elements of Informed Consent

In seeking informed consent the following information shall be provided to each subject (§46.116, 21CFR50, 21CFR56):

- ⇒ A statement (introduction) that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental [§.116(a)(1)] [§.50.25(a)(1)].
- ⇒ Possible Risks/Discomforts - state any known risks, side effects [§.116(a)(2)] [§.50.25(a)(2)]. In double-blinded studies, risks or possible reactions should be listed separately for each agent in each arm of the study.
- ⇒ Possible Benefits - describe potential benefits which might be expected by the subject and society in general [§.116(a)(3)] [§.50.25(a)(3)]. If the individual will receive no benefit this must be stated.
- ⇒ Financial Costs - list possible financial costs to participant [§.50.25(b)(3)]
- ⇒ A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject [§.116(a)(4)] [§.50.25(a)(4)]. If there are no alternatives, so state. (If there are alternatives, please describe them.)
- ⇒ Confidentiality - A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained [§.116(a)(5)] [§.50.25(a)(5)].
- ⇒ Voluntary Participation - note that participation is voluntary and subject may refuse to participate with no penalties [§.50.25(a)(8)]. List point of contact by name and phone number to call to terminate participation [§.116(a)(7-8)] [§.50.25(a)(7)] (two names and two different telephone numbers are required).
- ⇒ For research involving more than minimal risk, an explanation as to whether any compensation [§.50.25(a)(3)] and an explanation as to whether any medical treatments are available if injury occurs [§.50.25(a)(6)], and if so, what they consist of, or where further information may be obtained [§.116(a)(6)]
- ⇒ Injury / Complications - An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject [§.116(a)(7)] [§.50.25(a)(7)]. Describe in detail how complications will be handled.

- ⇒ A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled [§.116(a)(8)] [§.50.25(a)(8)].
- ⇒ Consent - by signing the consent form, the subject certifies that the document has been read to them, that they understand and that they have received a copy. The individual has been given the opportunity to ask questions and to discuss participation with the investigator.
- ⇒ Signatures / Dates - Each page of the informed consent must be date-stamped and initialed by the IRB Chair or Coordinator and initialed by the subject.

Additional Elements of Informed Consent

Additionally, one or more of the following elements of information must also be provided to each subject if required as indicated below:

- ⇒ The consent process must include a statement that the particular treatment or procedure may involve risks to the participant which are currently unforeseeable **UNLESS** the risk profile of all research-related interventions is well known **and** the research involves no investigational drugs or devices.
- ⇒ The consent process must disclose that the particular treatment or procedure may involve risks to the embryo or fetus, if the participant is or may become pregnant, which are currently unforeseeable **UNLESS** the research excludes women of child bearing potential and pregnant women **or** the risk profile of all research interventions or interactions on embryos and fetuses is foreseeable or there is no reasonable expectation that this research causes risks to fetuses or embryos.
- ⇒ The consent process must disclose anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent **UNLESS** there are no anticipated circumstances under which the participant's participation will be terminated by the investigator without regard to the participant's consent.
- ⇒ The consent process must disclose any additional costs to the participant that may result from participation in the research **UNLESS** there are no costs to the participant that may result from participation in the research.
- ⇒ The consent process must disclose the consequences of a participant's decision to withdraw from the research **and** procedures for orderly termination of participation by the subject **UNLESS** there are no adverse consequences (physical, social, economic, legal, or psychological) of a participant's decision to withdraw from the research.
- ⇒ The consent process must disclose that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant **UNLESS** significant new findings during the course of the research which may relate to the participant's willingness to continue participation are unlikely.
- ⇒ The consent process must disclose the approximate number of participants involved in the study **UNLESS** the approximate number of participants involved in the study is not important to a decision to take part in the research.

VA Required Paragraphs

The only informed consent document that the VA can recognize is the VA Form 10-1086. A VA Form 10-1086 must be used as the consent form for all VA research. The VA Form 10-1086 must incorporate all the elements required by regulations. In addition, the following statements are required to be inserted in VA 10-1086s.

- ⇒ VA 10-1086 must contain this statement if the research involves an investigational drug with an IND or a medical device with an IDE) A verbatim statement: "I have been told because this study involves articles regulated by the FDA, the FDA may inspect research identifying me as a subject of this investigation."
- ⇒ VA 10-1086 consents must contain a statement that a veteran—subject will not be required to pay for care received as a subject in a VA research project except if they are in an eligibility category that requires they pay a co-pay for medical services that are not part of the study.

Example 1: "You will not be charged for any treatments or procedures that are part of this study. However, if you are required to make co-payments for services provided by the VA or if you receive treatment that is part of your usual medical care, you or your third-party payer (e.g., insurance company) may be billed."

- ⇒ In the confidentiality section, the 10-1086 must include a statement that the Government Accounting Office (GAO), the ETSU/VA IRB, R&D, FDA, OHRP, DHHS, ORO, and any other applicable institutions may have access to the records.
- ⇒ VA 10-1086 must contain this Injury/Complications paragraph "According to VA Regulations [38CFR17.85(a)] the medical facility shall provide necessary medical care to a research subject injured as a result of participation in a research project. However, no additional compensation has been set aside. You have not waived any legal rights or released the VA or its agents from liability for negligence by signing this form."
- ⇒ VA 10-1086 must contain this statement required for veteran subjects "If you are a veteran taking part in a research study at the James H. Quillen VAMC, a copy of your signed/dated consent form will be placed in your medical record."
- ⇒ VA 10-1086 must contain an adequate description of any payment. (must include timing; method of payment; and if subject is being paid by VA check through Austin, the informed consent must note that the social security number will be required to process the check and that payments of any amount will be reported to the IRS and may be counted as income)
- ⇒ VA 10-1086 must contain this statement if the researcher believes that bodily fluids, substances or tissues of a research subject could lead to the development of a commercially valuable product "I authorize the use of my bodily fluids, substances or tissues for research purposes."

- ⇒ VA 10-1086 must contain Signature and date lines for the following
- subject or the subject's legally-authorized representative,
 - witness whose role is to witness the subject's or the subject's legally-authorized representative's signature, and
 - person obtaining the informed consent
- ⇒ VA consents must include information about where and how a veteran could verify the validity of a study and authorized contacts.

For VA studies, in the event that someone other than the investigator will be conducting the consent interview or obtaining consent, the investigator must provide a formal delegation of the responsibility of obtaining informed consent. The delegate must have received appropriate training (completed CITI IRB requirements as well as protocol-specific training by the PI).

The informed consent form must be signed and dated by the subject or the subject's legally authorized representative, a witness whose role is to witness the subject's or the subject's legally authorized representative's signature and the person obtaining the informed consent.

Compensation

Compensation in the form of payments to subjects for their participation in a research study must be IRB approved. The amount must be commensurate with the expected contributions of the subject. The amount and terms of the payment (check or cash, etc, as well as timing of receipt of compensation) must be stated precisely. The Informed Consent form should reflect a fair and appropriate amount that does not place undue pressure (coercion) on the volunteer.

For Non-English Speaking Subjects

Regulations require that informed consent be obtained in a language that is understandable to the subject (or to the subject's legally authorized representative). Validated translations of consent forms must be available for non-English speaking subjects. To address possible questions or concerns raised by the prospective subject, a qualified translator must be present and may act as a witness. Documentation of the qualifications of the translator must be added to the research records and available for administrative or QI auditing upon request.

When a full-length ICD embodying all the required elements is required by the IRB to document the consent process, that form must be written in a language understandable to the subject. The IRB requires that the appropriately translated ICD be submitted to the IRB for review and approval prior to their use in enrolling subjects. When informed consent is documented in accordance with HHS regulations at 45 CFR 46.117 (b) (1), the written ICD should embody, in language understandable to the subject, all elements necessary for legally effective informed consent.

The IRB may use expedited review procedures in approving such documents if the English language ICD has already been approved, and the investigator attests in writing to the accuracy of the translation.

Telephone Consenting is Not Recommended

For non-VA Studies, an investigator may, however, conduct a preliminary telephone interview to query a participant's interest in possibly participating in the research. If initial contact with prospective study subjects is to be made by telephone, a script of the phone contact is to be reviewed and approved by the IRB prior to use. Similarly if initial contact is to be made by mail, the content of the mailing script and list must be reviewed and approved by the IRB prior to initiation.

Following the telephone interview, and under certain circumstances (to be determined by the IRB with evidence of need), the investigator can fax an IRB approved informed consent document to the participant for his or her review. Documentation of this process is critical. The signature page must be witnessed by an individual known to the IRB or notarized, and reflect both the date and time of each signature. Enrollment may begin once the Principal Investigator receives a copy of the signed and notarized consent document. The original document must be immediately (within 24 hours) forwarded to the study file or patient record as appropriate, to be placed in the patient's medical record upon discharge. The date and time that the consent document (signed, notarized original copy) was entered into the patient chart must additionally be noted in the progress notes.

For VA Studies, during the recruitment process, researchers must make initial contacts with veterans in person and/or by letter prior to telephone contact and provide a telephone number or other means the veteran can use to verify the validity of the study, (one source of information is <http://www.clinicaltrials.gov>).

Legally authorized representative

A legally authorized representative shall be an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. Legally authorized representative is synonymous with legally acceptable representative. [21 CFR §50.3(l)] [45 CFR §46.102(c)]. A signature line for legally authorized representatives may only be included on the consent document if the IRB approves the enrollment of participants based on the permission of a legally authorized representative.

For cognitively impaired veterans subjects who would be enrolled in research studies at a Department of Veteran Affairs Facility, permission is obtained from a health care agent appointed by the person in a Durable Power of Attorney for Health Care (DPAHC) or similar document, court-appointed guardians of the person, or from next-of-kin in the following order: Spouse, Adult child (18 years or older), parent, adult sibling (18 years or older), grandparent, or adult grandchild (18 years or older).

For non-VA studies, in the case of an incompetent individual or an individual who lacks decision-making capacity, the individuals' health care decision maker (LAR) is designated in order of preference as one of the following:

A. Court-appointed Conservator or Guardian of the individual with authority to make health care decisions for the patient

B. Person named in the patient's Durable Power of Attorney for Health Care (DPAHC)

C. If the patient does not have a court-appointed guardian or conservator, AND does not have a person authorized to act under a Durable Power of Attorney for Health Care, then both of the following must be true for the individual identified to serve as the surrogate decision-maker for this patient:

1. The person identified above is an adult who has exhibited special care and concern for the patient, who is familiar with the patient's personal values AND who is reasonably available to serve as a surrogate.

2. It appears as though the person can make health care decisions for the patient in accordance with the patient's individual health care instructions, if any, and other wishes, if known to the health care decision maker. IF the patient has not given individual health care instructions, and the patient's specific wishes are not known, the health care decision maker can make a determination of the patient's desires or best interests in light of the patient's personal values and beliefs to the extent they are known.

This person may include, in order of descending preference, the patient's spouse, the patient's adult child, the patient's parent, the patient's adult sibling, any other adult relative of the patient or another adult who satisfies the requirements listed above.

The investigator must indicate in the application that he/she is requesting to utilize consent of a health care decision maker. The IRB must approve the use of an LAR. The IRB will review the rationale for this request, and ensure there are appropriate safeguards in place.

In addition, if research involving adults who are unable to consent is being conducted outside of the state of Tennessee, the investigator must consult Legal Counsel about which individuals are "legally authorized representatives" when the research is conducted in that jurisdiction. Researchers must submit a copy of this legal opinion to the IRB.

Investigators must obtain a copy of the court order if a court appointed conservator or guardian gives consent. Investigators must obtain a copy of the DPAHC if Person named in the patient's Durable Power of Attorney for Health Care (DPAHC) gives consent. In addition, if an individual identified to serve as the surrogate decision-maker for this patient gives consent, the investigator must document additional information evidencing the person's qualifications to serve as a surrogate. That information must include how long this person has lived with the patients, how long this person has known the patient and how often this person sees the patient, and any other evidence of the appropriateness of the selected surrogate.

Exculpatory language

Exculpatory language is prohibited. Informed consent, whether oral or written documents, may not contain any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, ETSU, VAMC or its agents from liability for negligence.

Requiring a Witness Signature on the Consent Form

The VA policy is that the VA form 10-1086 must be signed and dated by a witness whose role is to witness the subject's or the subject's legally authorized representative's signature.

The institution and the IRB reserve the right to require the signature of a witness on informed consent documents, as a matter of policy, under certain situations. Both the institution and the IRB have the authority to require protections for human subjects that exceed the minimum standards required under federal or state regulations. If the sponsor or the IRB require a witness to the consent process who also witnesses the signature, a note to that effect must be added to the consent document under the witness's signature line.

HIPAA Authorizations

When the HIPAA Authorization is embedded in the body of the ICD the IRB shall be responsible for reviewing both the content of the Authorization and its appropriateness to the research. When the HIPAA Authorization is attached to the ICD as an addendum (preferred), the IRB Chair, designee of the Chair, or the IRB Coordinator shall be responsible for the review.

Children

For participants < than 18 years of age, their parents or legal guardian are the legally authorized representative who may grant permission for their participation in research. When research is conducted in the state of Tennessee, children are all individuals under the age of 18 without exception.

According to the Tennessee Department of Children Services (DCS), applicable policies by virtue of the court order granting DCS legal custody of certain children (e.g., foster children) that department is the agency that is authorized to grant permission for participation in research in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCS. In such cases the PI must obtain a copy of the court order from DCS. The case manager (including the case manager's supervisor(s) or Regional Administrators' designee (s), the foster parent, and the contract agency caseworker are authorized by DCS to sign consent for routine medical care. DCS is authorized under Tennessee State law to consent to health care for the child, and therefore can serve as a guardian as defined in Subpart D.

Applicable State Laws regarding Reporting Requirements

Mandatory Reporting of Abuse. Any person who has knowledge of or is called upon to render aid to any child who is suffering from or has sustained any wound, injury, disability, or physical or mental condition is required to report the harm immediately by telephone to the:

- Judge having juvenile jurisdiction over the child;
- County office of the department;
- Sheriff of the county where the child resides; or
- Chief law enforcement official of the municipality where the child resides.
- The report will include (to the extent known) the name, address, and age of the child, the name address of the person responsible for the care of the child, and the facts requiring the report.

Mandatory Reporting of Sexually Transmitted Disease. Every physician or other person who makes a diagnosis of, treats or prescribes for a case of sexually transmitted disease designated as reportable is required to report the case immediately to the Department of Health. Reports include the name, address, age, sex, race, stage of disease, treatment, and control of the disease. Children 13 years of age or younger must be reported to the Department of Health. Reporting is required for children where sexual abuse is suspected regardless of injury to the Department of Health and the Department of Health will notify the Department of Children's Services.

Mandatory Reporting of Cancer. All laboratories, hospitals, facilities and practitioners are required to report to the Department of Health within 6 months of diagnosis any cancer in an individual if making the initial diagnosis. The report includes the diagnosis, occupation, family history and personal habits of the person diagnosed with cancer.

Because of these laws, IRB members must evaluate studies to determine whether disclosure of the implications of the laws is required for legally effective informed consent. Because of these laws, investigators must ensure that the consent process provides participants with accurate information concerning required reporting. Investigators are also responsible for compliance with these regulations.

Waiver of Informed Consent

DHHS provides for waiving or altering elements of informed consent under certain conditions [§.116(c)-(f)]. FDA has no such provisions because the types of studies that would qualify for waiver or alteration are either not regulated by FDA or are covered by the Emergency Treatment provision of FDA Regulation 21 CFR 50.23.

Waiver of informed consent can not be given when research is subject to FDA regulation.

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent provided one of the following sets of conditions exists and is documented:

⇒ 45 CFR 46.116(c) (Must meet one of the following criteria from section 1 as well as criteria number 2)

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine at least one of the following :
 - (a) public benefit or service programs; **or**
 - (b) procedures for obtaining benefits or services under these programs; **or**
 - (c) possible changes in or alternatives to those programs or procedures; **or**
 - (d) possible changes in methods or levels of payment for benefits or services under those programs

AND

2. the research could not practicably be carried out without the waiver or alteration.

⇒ 45 CFR 46.116(d) (Must meet all four criteria detailed below)

- a. The research involves no more than minimal risk to the subjects; **and**
- b. The waiver or alteration will not adversely affect the rights and welfare of the subjects **and**
- c. The research could not practicably be carried out without the waiver or alteration **and**
- d. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

If a waiver is granted, the minutes will document both the justification for and the approval of the waiver, along with any controverted issues raised by the IRB.

A waiver of parental permission (or student consent if the student is an adult) may not be granted if the study involves funding from the Department of Education and the study involves a survey, analysis, or evaluation that reveals information concerning the following categories:

- (1) political affiliations or beliefs of the student or the student's parent;
- (2) mental or psychological problems of the student or the student's family;
- (3) sex behavior or attitudes;
- (4) illegal, anti-social, self-incriminating, or demeaning behavior;
- (5) critical appraisals of other individuals with whom respondents have close family relationships;
- (6) legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers;

- (7) religious practices, affiliations, or beliefs of the student or student's parent; or
- (8) income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program),

In addition, all instructional materials, including teacher's manuals, films, tapes, or other supplementary material which will be used in connection with any survey, analysis, or evaluation as part of any applicable program shall be available for inspection by the parents or guardians of the children.

Waiver of Documentation of Informed Consent

Under certain conditions, the IRB can waive the requirement that the subject sign the consent form. However, waiver of documentation of informed consent does not constitute waiver of informed consent. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either (46 CFR 117(c):

- ⇒ That the only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

OR

- ⇒ that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases where the documentation requirement for informed consent is waived, the IRB may require the investigator to provide participants with a written statement regarding the research.

In addition, the IRB minutes will document required determinations regarding waiver of requirement for written documentation of informed consent. The minutes will also document the protocol specific findings justifying the determinations.

Observation of the Consent Process

Per 45 CFR 46, the IRB has the authority to observe or have a third party observe the consent process.

Situations where observation of informed consent may be requested include:

- ⇒ Studies where the capacity of the participant to provide informed consent may be questionable
- ⇒ Previous investigator serious or continuing non-compliance
- ⇒ High risk studies, such as Phase I trials
- ⇒ Complaint(s) received about the informed consent process
- ⇒ Any others as determined necessary by the IRB

Health Insurance Portability and Accountability Act (HIPAA)

HIPAA : The Health Insurance Portability and Accountability Act (HIPAA), also referred to as the Privacy Rule, at 45 CFR parts 160 and 164, establishes a category of health information, defined as protected health information (PHI), which a covered entity may only use or disclose to others in certain circumstances and under certain conditions.

In general, the Privacy Rule requires an individual to provide his/her signed permission, known as an Authorization, under section 164.508 of the Privacy Rule, before a covered entity can use or disclose the individual's PHI for research purposes.

Privacy Board

Under certain circumstances, however, the Privacy Rule permits a covered entity to use or disclose PHI for research without an individual's Authorization. One way a covered entity can use or disclose PHI for research without an Authorization is by obtaining proper documentation of a waiver of the Authorization requirement by the IRB, or another type of review body, known as a Privacy Board. The ETSU/VA IRB shall serve as the Privacy Board.

Pre-screening Activities

Pre-screening activities, without the use of an Authorization, are permitted under HIPAA [45 CFR 164.512(i)(1)(ii)]. Pre-screening activities involving prospective subjects, conducted to prepare a research protocol, or to enroll (or exclude) subjects from participation must be documented in the study file whether or not the subject meets the inclusion criteria or not. The Waiver of Informed Consent: Documentation of screening (pre-enrollment) activity only form, (available online) or a similar instrument may be used for this purpose. Note: VHA policy is more restrictive regarding activities preparatory to research. Accessing patient records for recruitment into research requires prior approval, waiver of authorization, even for a VA researcher's own patients.

Direct Identifiers (18 HIPAA Identifiers)

When developing research protocols, the Investigator must take into consideration allowable use and disclosure of PHI under HIPAA. The following identifiers are considered links to a particular individual or data that could enable individual identification:

- ⇒ names;
- ⇒ geographic subdivisions smaller than a State, including street address, city, county, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of a ZIP code;
- ⇒ all elements of dates (except year) for dates directly related to an individual (e.g., date of birth, admission);
- ⇒ telephone numbers;
- ⇒ fax numbers;
- ⇒ electronic mail addresses;
- ⇒ social security numbers;
- ⇒ medical record numbers;

- ⇒ health plan beneficiary numbers;
- ⇒ account numbers;
- ⇒ certificate/license numbers;
- ⇒ vehicle identifiers and serial numbers, including license plate numbers;
- ⇒ device identifiers and serial numbers;
- ⇒ web universal locators (URL's);
- ⇒ internet protocol (IP) address numbers;
- ⇒ biometric identifiers, including finger and voiceprints;
- ⇒ full-face photographic image and any comparable images; and
- ⇒ any other unique identifying number, characteristic, or code.

IRB Authority

The IRB has the authority to approve a waiver or an alteration of the Privacy Rule's Authorization requirement in addition to the traditional IRB authorities to protect research participants from risks under 45 CFR part 46 (Department of Health and Human Services (HHS) Regulations for the Protection of Human Subjects) 38 CFR 16, and 21 CFR parts 50 and 56 (Food and Drug Administration (FDA) Regulations on Protection of Human Subjects). Other Federal and State laws and regulations may impose other or additional restrictions and limitations on the use of health information for research that may not be waived or altered by an IRB (or Privacy Board) under the authority granted to it by the Privacy Rule. The IRB and the OPHRS shall enforce the mandates of the Privacy Rule pursuant to the requirements necessary for the protection of the subject and/or their protected health information as applicable to the research.

Training

Training on the requirements imposed by the Privacy Act and other information regarding HIPAA, including guidance, forms and continuing education, will be made available to researchers online.

Levels of IRB Review

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:

- ⇒ Exempt from IRB Committee Review
- ⇒ Expedited Review
- ⇒ Full Review

 **No Human participants may be enrolled or recruited prior to receipt of written final approval of the application from the IRB.**

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, either the Vice Chair or the Vice Provost for Research at East Tennessee State University 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). In the absence of the Chair or Vice Chair, the Vice Provost for Research, or the Associate Chief of Staff for Research will review the determination. 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 will then be submitted for either expedited or full review, as appropriate to the level of risk, by 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 all human subject protections and 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. If the study includes interactions with participants, there is 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
 - d. the name and contact information for the investigator
5. The research has adequate provisions to maintain the privacy interests of participants.

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

Categories

Only studies that meet the six specific categories of exempt activities as delineated by HHS 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.

Categories for Exempt Approval:

1. 45 CFR 46.101 (b)(1): Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
 - a. research on regular and special education instructional strategies, or
 - b. research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. 45 CFR 46.101 (b)(2): Research involving the use of educational tests, (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
 - a. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **and**
 - b. any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation or insurability.

For 45 CFR 46 (101) (b)(2), the exemption for research involving survey or interview procedures or observations of public behavior DOES NOT apply to research covered by 45 CFR Part 46, Subpart D (Additional DHHS Protections for Children Involved as Subjects in Research), except for research involving observation of public behavior where the investigators do not participate in the activities being observed. .

3. 45 CFR.46.101(b)(3): Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under 45 CFR 46.101(b)(2)) if:
 - a. the human subjects are elected or appointed public officials or candidates for public office, **or**
 - b. federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. 45 CFR 46.101(b)(4): Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

To qualify for the above 45 CFR 46 (101) (b) category 4 exemption, data, documents, records or specimens must already exist at the time the research is proposed.

5. 45 CFR 46.101(b)(5): Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
 - a. Public benefit or service programs;
 - b. procedures for obtaining benefits or services under those programs;
 - c. possible changes in or alternatives to those programs or procedures;
 - or**
 - d. possible changes in methods or levels of payment for benefits or services under those programs.

To qualify for Exemption 5 for Public Benefit Projects, which is for projects conducted by or subject to approval of federal agencies, the following criteria must be satisfied:

- ⇒ The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive or nutrition services as provided under the Older Americans Act)
- ⇒ The research or demonstration project must be conducted pursuant to specific federal statutory authority
- ⇒ There must be no statutory requirement that the project be reviewed by an IRB
- ⇒ The project must not involve significant physical invasions or intrusions upon the privacy of participants
- ⇒ Authorization or concurrence by funding agency

6. 45 CFR 46.101(b)(6) and 21 CFR 56.104(d): Taste and food quality evaluation and consumer acceptance studies,
 - a. if wholesome foods without additives are consumed **or**
 - b. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the US Department of Agriculture.

If the proposed research activities do not meet the criteria for exemption, the IRB will promptly correspond with the investigator outlining any additional information needed and proper type of review (e.g., expedited or full)

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, certain research, meeting the specified criteria, may be reviewed by the IRB Chairperson, Vice Chair or two or more IRB members who have been selected based on their expertise and experience, not at a convened Committee meeting.

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

- X** research is minimal risk but does not appear in one of the listed categories
- X** research involves greater than minimal risk.
- X** 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.
- X** research is classified and involves human subjects.

Categories

HHS Regulations at 45CFR.46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register at 63 FR 60364-60367. The following categories of research may be reviewed by the IRB through an expedited review procedure:

Only those research activities that:

- ⇒ present no more than minimal risk to human subjects **AND**
 - ⇒ 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](#) :
1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
 - a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

- b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
 - a. from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; **or**
 - b. from other adults and children², considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means.

Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(4\)](#). This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. [45 CFR 46.101\(b\)\(2\)](#) and (b)(3). This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows:
 - (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; **or**
 - (b) where no subjects have been enrolled and no additional risks have been identified; **or**
 - (c) where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

² Children are defined in the HHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted."

Expedited reviews should be conducted with the same depth as reviews conducted by the convened board. Research materials submitted must include sufficient detail for the reviewer(s) to determine the study meets criteria 45 CFR 46.111, 21 CFR 56.111 and 38 CFR 16.111, if applicable, for approval.

Expedited reviewers may approve research, require modifications in order to secure approval, or defer the proposal to the convened board. Protocols are also referred to the convened board if the investigator does not concur with the requested modifications.

If the proposal is approved or approved with stipulations, reviewers 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 expedited studies:

- Recommendations by another committee, such as the VA Research and Development Committee
- Consent being given by legally authorized representatives
- Identified conflict of interest of involved study personnel
- Research for which participants would be exposed to additional risk (i.e., disproportionate number or severity of unanticipated problems, Phase I study)

The full Committee is advised of research proposals/activities that have been approved through the expedited review procedure.

Full Reviews

For Initial Full reviews, see pages 16-21 of this handbook.

Amendments

It is the policy of both the ETSU IRB and the ETSU/VA IRB to review all requests for modifications to any previously approved research study (including exempt studies) to determine if the change will alter the risk/benefit ratio of the study. A complete description of the modification must be received prior to review. Modifications may include, but are not limited to, protocol amendments, changes in the number of subjects, changes in the informed consent, etc. All requested changes in the conduct of a study and/or changes to study documents must be approved by the IRB prior to implementation of that modification. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects [21 CFR 56.108(a)(4)]. In such a case, the IRB will be promptly informed of the change following its implementation (within 10 working days) and will review the change to determine that it is consistent with ensuring the subject's continued welfare. IRB members with a conflict of interest may provide information requested by the IRB, but may not participate in the deliberation or vote of the IRB on the involved modification.

Modifications Requested by Sponsor

If the modification is requested by the sponsor, a copy of any pertinent correspondence from the sponsor must be submitted with the Modification Request Form. In addition, investigators must submit any proposed revised documents with the Modification Request Form.

Reconsenting/Notification of Participants

If the modification warrants changes to the informed consent document, the investigator must address whether the information needs to be communicated to currently or previously enrolled participants, and if so, how it will be communicated. This may be accomplished by using an addendum to the initial ICD or by re-consenting the subject using the modified ICD. While the investigator is responsible for making the initial decision regarding any necessary document changes, the IRB will make the final determination of whether the modification requires a change to the ICD or other study documents. The IRB will also make the final determination of the necessity of re-consenting of currently enrolled participants or notification of participants who have completed research interventions.

Minor Modifications

The initial request as to whether a modification alters risks to the participants is made by the Principal Investigator. The modification is received by the Coordinator and presented it to the Chair for his/her review. The Chair is responsible for evaluating the change in procedures and risks, and determining whether full IRB review of the modification is necessary.

Proposed changes for previously approved research that are classified as minor modifications may be reviewed and approved in an expedited manner by the IRB Chair or, in the case of the Chair's absence or conflict of interest, his/her Designee. The designee should be one or more experienced reviewers designated by the chairperson from among the IRB membership.

Examples of minor modifications may include, but are not limited to, the following:

1. Administrative changes, such as correction of typographical error(s)
2. Revision of phone number(s)

Non-Minor Modifications

When a modification is determined to be non-minor, the Chair or his/her designee serves as a primary reviewer. The IRB Committee receives a synopsis of the primary reviewer's findings at the convened meeting. The IRB must review and approve changes at a convened meeting* before changes can be implemented (*meeting at which a majority of the members are present, including at least one member whose primary concerns are non-scientific). At the Chair's discretion, the Principal Investigator may be required to present the non-minor modification to the convened board.

Examples of non-minor modifications may include, but are not limited to, the following:

- ⇒ Change in protocol procedures, such as increasing the number of times a test is performed or adding additional procedures
- ⇒ Deletion or decrease in tests performed as part of safety evaluations
- ⇒ The addition of serious unexpected adverse events or other significant risks to the ICD
- ⇒ Changes, which, in the opinion of the IRB Chair or his/her Designee, do not meet the definition of a minor modification
- ⇒ Any change that increases the risk of the study

Exempt Research

Any changes in an exempt study must be submitted to the IRB for approval prior to initiation of the change. The IRB Chair will determine if the modification renders the study ineligible for continuing exempt status; and if so, the modification will not be approved. The investigator will be notified in writing that he may withdraw the modification request and continue the study as previously determined to qualify under exemption guidelines or submit the study for appropriate review and approval through an expedited or full board review.

VA Studies

Modifications must also be submitted to the VA R&D Office, if the study involves VA patients, VA staff, VA resources, time or equipment. Any change in authorized prescribers of the investigational drug requires the submission of a revised 10-9012.

Changes in Study Sites or Investigators

Changes in study sites, investigators or revisions in study staff must also be reported to the IRB. These may require a cover letter, a revised Form 103, or, as applicable, a revised protocol. In the case of a change in the principal investigator, if at all possible, the letter should be signed by the investigator who holds the approval. The newly assigned investigator of a full review study however, must show proof of having obtained required education and submit a current CV for the purpose of assessment of qualifications. If the PI is unknown to the IRB, the PI must also attend a convened IRB meeting. The change will be noted in the minutes.

Continuing Review

Full Continuing Review

Studies initially reviewed by the full, convened IRB undergo continuing review by the full convened IRB with recorded vote on each study, unless the study has been modified such that it meets the federal guidelines to be eligible for reclassification for expedited continuing review. For full continuing review, the IRB reviews proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in the nonscientific areas (45 CFR 46.108(b)).

In conducting full continuing review, a Primary Reviewer System is utilized. Consideration for the selection of Primary Reviewers to serve is based on area(s) of expertise in compliment to the research under review, term of IRB membership, dedication to continuing education and availability to accept new and continuing research proposals. The Chair, Vice Chair review each continuing review submission to determine which members have the relevant expertise to conduct an in-depth evaluation of the protocol. Primary Reviewers are responsible for analyzing the protocol and the complete IRB application in detail and are authorized to discuss any unanswered questions with the investigators, associated researchers or consultants prior to or during the convened meeting.

For continuing review of research that does not qualify for expedited review, all IRB members receive for review:

1. Project Narrative, which serves as protocol summary
2. Continuing Review/Study Closure Application (Form 107), which serves as status report, and any attachments (complete documents as received from investigator).
3. Copy of the current approved informed consent document
4. Copy of any newly proposed consent document
5. Summary history of modifications reported to the IRB and list of interim adverse events, if applicable
6. Copy of any IRB and, if appropriate, VA audits that have occurred since last review

For continuing review of research that does not qualify for expedited review, the primary reviewer(s) receive for review:

1. Project Narrative, which serves as protocol summary
2. Continuing Review/Study Closure Application (Form 107), which serves as status report, and any attachments (complete documents as received from investigator).
3. Copy of the current approved informed consent document
4. Copy of any newly proposed consent document
5. AE Reports and summary history of modifications done since the last review
6. HIPPA authorization, if applicable
7. Copy of any IRB and, if appropriate, VA audits that have occurred since last review
8. Copy of the complete protocol, including any protocol modifications previously approved by the IRB

Upon request, any IRB member has access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting. In addition, any IRB member has access to additional information provided to individual reviewers

The full IRB Committee is informed of the Primary Reviewer's findings at a convened meeting. 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.

After discussion, including an explanation of the important issues that were evaluated, the full, convened board makes its determination with a recorded vote. Any controverted issues will be recorded in the minutes. This process allows the IRB to conduct a more substantive review and discussion at convened meetings.

Minutes of IRB meetings document separate deliberation, actions, and votes for each protocol undergoing continuing review by the convened board.

Expedited Continuing Review

Expedited continuing review may be conducted if the study was initially eligible for, and approved by, an expedited mechanism, with the following exception: if an amendment or continuing review indicates changes in the study so that it is now ineligible for expedited continuing review as noted with submission of modification/continuing review. The IRB is only permitted to use expedited review for the continuing review of research that involves solely one or more of the activities published at 63 FR 60364-60367. If the study is modified such that it fails to meet expedited criteria for review, the study will undergo full continuing review.

When conducting research under an expedited review procedure, the IRB Committee Chair or designated Expedited Reviewers conduct the review on behalf of the full IRB Committee. When performing continuing review by the expedited procedure, the IRB Chair or designated Expedited Reviewers receive for review all of the following documentation:

1. Project Narrative, which serves as protocol summary
2. Continuing Review, Study Closure Application (Form 107), which serves as status report, and all attachments (completed documents as received from investigator)
3. Copy of the current approved informed consent document
4. Copy of any newly proposed consent document
5. Copy of current HIPAA Authorization document
6. Complete protocol, including any protocol modifications previously approved by the IRB

Exempt Studies

Studies that have been determined to meet exempt status do not undergo continuing review unless a change in the study renders it ineligible for exempt status per federal guidelines. Investigators are informed in the exempt status letter to inform the IRB of any change in the project prior to its implementation, and reclassification under expedited or full review would be determined at that time by the IRB Chair.

Approval Criteria

Approval, both initial and continuing, must meet HHS regulations at 45 CFR 46.111, including determinations by the IRB regarding risks, potential benefits, informed consent and participant safeguards. Criteria for both initial and continuing review approval are the same and therefore, IRB continuing review must include a determination by the IRB that risks to subjects continue to be minimized, risks to subjects continue to be reasonable in relation to anticipated benefits, selection of subjects continues to be equitable, informed consent continues to be adequate, and appropriately obtained and documented; where appropriate, the research plan continues to make adequate provision for monitoring the data collected to ensure the safety of subjects; there continue to be adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, appropriate safeguards continue to be included to protect vulnerable participants. If interim changes in IRB policy have occurred such that the proposal submitted for continuing review would not be approved if the same study were an initial submission, the IRB does not approve the continuing review of that protocol.

Changes/New Information

The IRB is also responsible for ensuring that changes in approved research are promptly reported to, and approved by, the IRB [21 CFR 56.108(a)(3-4)]. Continuing review will include an IRB determination of whether new information or unanticipated risks have been discovered since the previous IRB review. Based on new information or unanticipated risk, the IRB has the authority to reconsider its approval, require modifications to the study, and/or revise the continuing review timetable. Any significant new findings which may relate to the subject's willingness to continue participation should be provided to the subjects in accordance with 21 CFR 50.25.

Review Interval

The policy of ETSU IRB and ETSU/VA IRB is to determine appropriate continuing review interval for each review conducted by the IRB. The IRB will generally obtain review more often than annually if any of the following situations are true:

1. Recommendations by another committee, such as the VA Research and Development Committee, to obtain review more often than annually
2. Consent being given by legally authorized representatives
3. Identified conflict of interest of involved study personnel
4. Research for which participants would be exposed to additional risk (i.e., disproportionate number or severity of adverse events, Phase I study) and study does not have DMSB
5. Previous suspension of the study due to non-compliance
6. Recommendations by other IRB members that review be conducted more often than annually

Informed Consent

IRB continuing review will also include evaluation of the informed consent document currently in use. The currently approved informed consent, as well as any proposed informed consent document, will be reviewed to determine if the information provided continues to be accurate and complete, and to determine if any new information needs to be added. The informed consent document will also be reviewed to ensure that any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5). Review of the informed consent document will take place not only at continuing review, but at other times when new information becomes available that needs to be communicated to participants.

Source Verification

When conducting continuing review, the IRB is responsible for determining which studies need verification from sources other than the investigator that no material changes in the research have occurred since the previous IRB review [21 CFR 56.108(a)(2)]. The need for additional verification will be determined by the IRB on a case-by-case basis. Source verification will be required when:

- ⇒ Investigator is providing inconsistent information that can not be resolved
- ⇒ The IRB doubts the investigator's veracity
- ⇒ IRB doubts that the investigator has sufficient relevant knowledge
- ⇒ IRB perceives that investigator is intentionally not providing necessary information

No Grace Period

Per regulations, there is **no** grace period that allows the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If any activity occurs or continues after the expiration date, the investigator is deemed to be out of compliance with both federal regulations and ETSU/VA policies.

The IRB may restrict, require modifications, or terminate a research project based on continuing review by the IRB Committee. All studies in which the IRB requests changes to current documents are assigned a pending status. IRB approval is not given until the requested changes are received and approved. **The expiration period is not extended.** If continuing review and re-approval fails to occur by the continuing date specified by the IRB, all research activities must **stop**, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.

If the IRB does not re-approve the research by the expiration date, the IRB approval expires. The PI, upon receipt of expiration letter, must immediately submit to the Chair a list of research participants that could be harmfully affected by expiration of the research. The IRB Chair, with appropriate consultation with (for VA) either the Chief of Staff (COS), or in his/her absence, the ACOS/R, or (for ETSU) the Vice Provost for Research (VPR), will determine if the subject(s) may continue in the research. If the ACOS/R or VPR is not a physician, they will designate a physician as a consultant. If the study is an FDA regulated study, the COS, ACOS/R or VPR and IRB Chair will follow FDA requirements in 21 CFR 56.108(b)(2) and (3) in making their decision.

Vulnerable Population

The ETSU and ETSU/VA IRB will consider certain groups of human subjects to be particularly vulnerable to coercion or undue influence in a research setting, to include children (also indirectly an infant, if mother nursing the infant is a subject of research), fetuses, pregnant women, mentally disabled (cognitively impaired) persons, prisoners, and economically or educationally disadvantaged persons. In reviewing research projects, the IRB will scrutinize those involving these vulnerable groups, to ascertain that their use is adequately justified and additional safeguards are implemented to minimize risks unique to each group.

The appropriate checklist(s) (Form 130-133 for children, Form 134 for pregnant women and fetuses, Form 135 for neonates, Form 136 for Prisoners, Form 137 for Waiver or Alteration of Requirement to Obtain Informed Consent, Form 138 for Waiver of Requirement for Written Documentation of Informed Consent) will be completed by the IRB Chair or Primary Reviewer. The IRB minutes will document the IRB's determinations required by the regulations for research involving children, pregnant women, fetuses, neonates, or prisoners. In addition, the IRB minutes will document required determinations regarding waiver of informed consent or waiver of documentation of informed consent. The minutes will also document the protocol specific findings justifying the determinations.

Any proposal engaging subjects of vulnerable categories, such as children, prisoners, pregnant women, handicapped or mentally disabled persons, will additionally be reviewed by one or more individuals who are knowledgeable about and experienced in working with these subjects.

The foremost ethical concern in research that involves individuals with psychiatric, cognitive, or developmental disorders, or who are substance abusers is that their disorders may compromise their capacity to fully understand the information presented by an investigator and their ability to make a reasonable decision about their participation. In certain circumstances, their eagerness for release may induce an institutionalized person, especially one who is involuntarily confined, to participate in research out of a desire to appear "rational" and "cooperative" to those who will make decisions about his or her release. It is imperative that the privacy and confidentiality of identifying information gathered in research delving into emotionally sensitive topics be strictly protected.

Research involving the Cognitively Impaired

Research involving persons with impaired decision-making capacity will only be approved when the following conditions apply:

- ⇒ Only incompetent persons or persons with impaired decision making capacity are suitable as research participants. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired-decision making capacity as participants. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.
- ⇒ The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

- ⇒ Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC)) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.
- ⇒ The IRB must make a determination in writing of each of these criteria. Investigators must submit a form 142. The IRB documents these determinations on form 143.
- ⇒ Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.
- ⇒ Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

Surrogate consent may be requested and accepted only when the prospective research participant is incompetent or has an impaired decision-making capacity, as determined and documented in the person's record. For VA studies, this must be documented in the person's medical record in a signed and dated progress note. The determination must be made in accordance with the following requirements. Refer to Informed Consent Policy for information about surrogate consenting.

- (a) The practitioner may determine after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. For VA studies, this determination must be made in consultation with the chief of service, or COS.
- (b) For VA studies only, consultation with a psychiatrist or licensed psychologist must be obtained when the determination that the prospective research subject lacks decision-making capacity is based on a diagnosis of mental illness.
- (c) The participant's surrogate must be provided all information that normally would be provided to a participant.
- (d) If feasible, the practitioner must explain the proposed research to the prospective research subject even when the surrogate gives consent. Under no circumstances may a subject be forced or coerced to participate in a research study.

Waiver of Assent

Waiver of Assent: The IRB may waive the requirement for assent of the subject when:

- ⇒ The capability of some or all of the subjects is so limited that they cannot reasonably be consulted;
- ⇒ In determining whether subjects are capable of assent, the IRB shall take into account the maturity, psychological state and physical state of the subjects involved.
- ⇒ This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate.
- ⇒ The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subject and is available only in the context of the research; or
- ⇒ IRB determines that the assent may be waived according to the same criteria by which consent may be waived.

If subjects enrolled in the research develop the capacity to provide informed consent, the IRB may require consent of the subject in accordance with 45 CFR 46.116. When the IRB determines that assent is required, assent shall be documented by having the subject sign and personally date the written informed consent.

Children

VA studies may not involve children.

Definitions

- ⇒ “Children” are persons who have not attained the legal age for consent to treatments or procedures involved in research, under the applicable law of jurisdiction in which the research will be conducted
- ⇒ “Assent” means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. (See Appendix Q). In determining whether children are capable of assenting, the investigator and the IRB must take into account the ages, maturity, and psychological state of the children involved [§.46.408(a)].
- ⇒ “Permission” means the agreement of parent(s) or guardian to the participation of their child or ward in research.
- ⇒ “Guardian” means an individual who is authorized under applicable State or Local law to give permission on behalf of a child to general medical care.
- ⇒ “Emancipated Minor” means a legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage or procreation. NOTE: In the state of Tennessee, the Age of Majority is 18 years of age.

Definitions continued

⇒ “Minimal Risk” means where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Assessment of Risks, Benefits

The IRB, when reviewing research involving children as participants, considers the risks, benefits, and discomforts in the proposed research and assesses their justification in light of the expected benefits. When assessing the risks and benefits, the IRB should weigh the circumstances of the children under study, the magnitude of risks that may accrue from the research, and the potential benefits to the child or to society. The assessment of the probability and magnitude of the risk may be different in sick children and may vary depending on the disease the child may have. When assessing possible benefits, the IRB must also consider the variability in health statuses, taking into account the current health status and the likelihood of progression to a worsened state without the research intervention.

Federal regulations require the IRB to classify research involving children into one of four categories and to document discussion of the risks and benefits of the research study. Those four categories of research are as follows:

1. Research not involving greater than minimal risk (45 CFR 46.404): The IRB may approve research involving children and not involving greater than minimal risk, provided that the IRB finds and documents that:
 - No greater than minimal risk to children is presented; and
 - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405): The IRB may approve research involving children in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is likely to contribute to the participant's well-being, only if the IRB finds that:
 - The risk is justified by the anticipated benefit to the participant;
 - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches; and
 - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects disorder or condition (45 CFR 46.406): The IRB may approve research involving children in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure that is not likely to contribute to the participant's well-being, only if the IRB finds that:
- The risk represents a minor increase over minimal risk;
 - The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition that is of vital importance for the understanding or amelioration of disorder, or condition; and
 - Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.
4. If an IRB does not believe that research within the scope described in §§50.1 and 56.101 of this chapter and involving children as participants meets the requirements of §50.51, §50.52, or §50.53, the research may proceed only if: [45 CFR §46.407] [21 CFR §50.54]
- The IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
 - The agency head, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either:
 - ◇ That the research in fact satisfies the conditions of 45 CFR §46.404, §46.405, or §46.406 {FDA: 21 CFR §50.51, §50.52, or §50.53}, as applicable, or
 - ◇ That the following conditions are met:
 - ◆ The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
 - ◆ The research will be conducted in accordance with sound ethical principles.
 - ◆ Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in 45 CFR §46.408 {FDA: 21 CFR §50.55}.

In all cases, the IRB must determine that adequate provisions have been made for soliciting the assent of children and the permission of the parents or guardians.

Consent and Assent

Regulations require that the IRB determine that adequate provisions are made for obtaining and documenting the assent of the children, when in the judgment of the IRB, the children are capable of providing assent. In determining whether children are capable of assent, the IRB shall take into account the age, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in the research under a particular protocol, or for each child, as the IRB deems appropriate. When the IRB determines that assent is required, it will also determine whether and how assent must be documented .

Waiver of Assent

The IRB may waive the requirement for assent of some or all of the children when:

- ⇒ The capability of some or all of the children is so limited that they cannot reasonably be consulted **OR**
- ⇒ The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research

Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement if it finds and documents that:

- ⇒ The research involves no more than minimal risk to the participants;
- ⇒ The waiver will not adversely affect the rights and welfare of the participants;
- ⇒ The research could not practicably be carried out without the waiver; and
- ⇒ Whenever appropriate, the participants will be provided with additional pertinent information after participation

In addition, the IRB shall require the permission of each child's parents or guardian.

Only the parents may grant permission for their child's participation in research. Assent is to sought from the child only after permission has been obtained from the parent(s). Grandparents and other relatives may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the PI must obtain a copy of the court order as evidence of that person's authority.

When parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 or 45 CFR 46.405 (categories 1 and 2 above—Research not involving greater than minimal risk and research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects). For research covered by 45 CFR 46.406 and 45 CFR 46.407, (greater than minimal risk and no direct benefit or otherwise unapprovable) and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Permission by parents or guardians will be documented appropriately.

Wards of the state

Children who are wards of the State or other agency, institution, or entity can be included in research approved under 45 CFR 46.406 (number three above) or 45 CFR.407 (number four above) only if such research is either 1) related to their status as wards or 2) be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. In research approved under 45 CFR 46.406 (number three above) or 45 CFR.407 (number four above), the IRB must require appointment of an advocate for each child who is a ward. This advocate serves in addition to any other individual acting on behalf of the child as a guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization. The IRB documents determinations regarding children as wards on Form 131.

Research Involving Pregnant Women, Fetuses and Neonates

It is the policy of the IRB to provide additional protections for pregnant women, fetuses and non-viable neonates involved in research. The IRB does not allow pregnant women, fetuses or non-viable neonates to be involved in research without specific approval of their involvement in the research (e.g., consultation with professionals in the field).

1. **Research involving pregnant women or fetuses:** The IRB may approve research involving pregnant women or, fetuses only if the IRB finds and documents that all of the following conditions are met:
 - ⇒ Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
 - ⇒ The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
 - ⇒ Any risk is the least possible for achieving the objectives of the research;
 - ⇒ If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of 45 CFR 46.

- ⇒ If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A (DHHS) except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest.
- ⇒ Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- ⇒ For children as defined in 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of 45 CFR 46.
- ⇒ No inducement, monetary or otherwise, will be offered to terminate a pregnancy.
- ⇒ Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
- ⇒ Individuals engaged in the research will have no part in determining the viability of a neonate.

In addition, for VA Studies involving pregnant women, the following criteria must be met:

- ⇒ Adequate provision has been made to monitor the risks to the participants and the fetus.
- ⇒ Adequate consideration has been given to the manner in which potential participants are going to be selected, and that adequate provision has been made to monitor the informed consent process such as:
 - Overseeing the actual process by which individual consents are secured either by approving enrollment of each individual into the activity, or by verifying, perhaps through sampling, that approved procedures for enrollment into the activity are being followed; and
 - Monitoring the progress of the activity and intervening, as necessary, through steps such as visits to the activity site and continuing evaluations to determine if any unanticipated risks have arisen.

In addition, for VA studies, activities related to pregnant women must not be undertaken unless the purpose of the activity is to meet the health needs of the mother or the particular fetus, the risk to the fetus is minimal, and in all cases, is the least possible risk for achieving the objectives of the activity. Individuals engaged in the activity will have no part introducing any procedural changes, for the research purposes, into the procedures for terminating the pregnancy.

Research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue), must not be conducted by VA investigators, while on official duty, or at VA facilities, or at approved off-site facilities.

Research related to in-vitro fertilization must not be conducted by VA investigators, while on official duty, or at VA facilities, or at approved off-site facilities.

2. Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

- ⇒ Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

- ⇒ Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
- ⇒ Individuals engaged in the research will have no part in determining the viability of a neonate.
- ⇒ The requirements of paragraph (b) or (c) of 45 CFR 46.205 have been met as applicable.

3. **Neonates of uncertain viability:** Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by subpart B unless the following additional criteria have been met:

- ⇒ The IRB determines that:
 - The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
 - The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
 - The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

4. **Nonviable neonates:** After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

- ⇒ Vital functions of the neonate will not be artificially maintained;
- ⇒ The research will not terminate the heartbeat or respiration of the neonate;
- ⇒ There will be no added risk to the neonate resulting from the research;
- ⇒ The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- ⇒ The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of Sec. 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

5. **Viable neonates.** If a neonate is judged viable (i.e., likely to survive to the point of sustaining life independently, given the benefit of available medical therapy), it is then called an infant and should be treated as a child for purposes of research participation. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of 45 CFR 46.

Research involving, after delivery, the placenta, the dead fetus or fetal material

1. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities. Tennessee Code Annotated section 39-15-208 makes it unlawful for any person or entity to engage in the following activities without the prior knowledge and consent of the mother:
- *medical experiments,*
 - *research, or*
 - *taking of photographs upon an aborted fetus.*

Additionally, no person or entity may offer or accept money or anything of value for an aborted fetus. Violations of these provisions are punishable as a Class E felony .

2. If information associated with material described in paragraph A of 45 CFR 46.206 is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of the regulations are applicable.

Human Fetal Tissue

1. Human fetal tissue may be used only if the woman providing the tissue makes a statement, made in writing and signed by the woman, declaring that: [42 USC §498A(b)(1)]
- ⇒ The woman donates the fetal tissue for use in research.
 - ⇒ The donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue.
 - ⇒ The woman has not been informed of the identity of any such individuals.
2. Human fetal tissue may be used only if the attending physician with respect to obtaining the tissue from the woman involved makes a statement, made in writing and signed by the physician, declaring that: [42 USC §498A(b)(2)]
- ⇒ In the case of tissue obtained pursuant to an induced abortion:

- The consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research.
- No alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue.
- The abortion was performed in accordance with applicable State law.

⇒ The tissue has been donated by the woman in accordance with 42 USC §498A(b)(1).

⇒ Full disclosure has been provided to the woman with regard to:

- Such physician's interest, if any, in the research to be conducted with the tissue.
- Any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care.

Human fetal tissue may be used only if the individual with the principal responsibility for conducting the research involved makes a statement, made in writing and signed by the individual, declaring that the individual: [42 USC §498A(c)]

⇒ Is aware that:

- The tissue is human fetal tissue.
- The tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth.
- The tissue was donated for research purposes.

⇒ Has provided such information to other individuals with responsibilities regarding the research;

⇒ Will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and

⇒ Has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purposes of the research.

46.207: Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates.

The Secretary of the Department of Health and Human Services (DHHS) will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if:

⇒ The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

⇒ §The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

- That the research, in fact, satisfies the conditions of §46.204, as applicable; or
- The following:
 - ◇ The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and
 - ◇ The research will be conducted in accord with sound ethical principles; and
 - ◇ Informed consent will be obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46
 - ◇

Research in which the subject is a fetus, in-utero or ex-utero (including human fetal tissue), must not be conducted by VA investigators, while on official duty, or at VA facilities, or at approved off-site facilities.

Research related to in-vitro fertilization must not be conducted by VA investigators, while on official duty, or at VA facilities, or at approved off-site facilities.

Research Involving Prisoners

The provisions of 45 CFR 46 Subpart C provide additional protections to biomedical and behavioral research involving prisoners as participants. These safeguards apply to research where any participant is or becomes a prisoner.

A prisoner is defined by HHS regulations at 45 CFR 46.303 as “any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”

Research involving prisoners must not be conducted by VA investigators while on official duty, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer.

Required IRB Composition

Whenever the IRB reviews 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 prison(s) involved, apart from their membership on the IRB;
- ⇒ At least one voting IRB member present at the meeting must be a prisoner, or a prisoner advocate /representative with appropriate background and experience to serve in that capacity.

These composition requirements must be met for all types of review of the protocol, including initial review, continuing review, review of protocol modifications, and review of unanticipated problems involving risks to participants.

Additional IRB Duties

In addition to all other pertinent requirements, the IRB may approve research involving prisoners only if the IRB finds and documents that all of the following conditions are met:

1. The research under review represents one of the following categories of permissible research (45 CFR 46.306):
 - ⇒ Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk* for prisoners and no more than inconvenience to the subjects;
 - ⇒ Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk for prisoners and no more than inconvenience to the subjects;
 - ⇒ Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults); provided that the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research;** **or**
 - ⇒ Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.**

⇒ Research that involves epidemiologic studies that meet the following criteria: [45 CFR §46 Waiver of the Applicability of Certain Provisions of Department of Health and Human Services Regulations for Protection of Human Research Subjects for Department of Health and Human Services Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects (Federal Register, Vol. 68, No. 119, pp. 36929-36931, Friday, June 20, 2003)] where

1. The sole purposes of the research are one of the following:
 - To describe the prevalence or incidence of a disease by identifying all cases or;
 - To study potential risk factor associations for a disease.
2. The institution responsible for the conduct of the research certifies to the Office for Human Research Protections, DHHS, acting on behalf of the Secretary that the IRB approved the research and fulfilled its duties under 45 CFR §46.305(a)(2)–(7) and determined and documented that: (Note: Certification to OHRP is required only for research conducted or sponsored by DHHS. IRBs still have to make and document the required findings.)
 - The research presents no more than minimal risk and no more than inconvenience to the prisoner-participants.
 - Prisoners are not a particular focus of the research.

* Note that the definition of minimal risk for prisoner at 45 CFR 46.303(d) differs from the definition of minimal risk for other research: For prisoner: the definition of minimal risk is the “probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.”

** Refer to section C, Research Conducted or Supported by DHHS

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides to the IRB justification in writing for following some other procedures, control subject must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
5. The information is presented in language which is understandable to the subject population;
6. Adequate assurance exists that parole boards will not take into account a prisoner’s participation in the research in making decision regarding parole; and each prisoner is clearly informed in advance that participation in the research will have no effect of his or her parole; and

7. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual's sentences, and for informing participants of this fact.

Research conducted or supported by DHHS

For research conducted or supported by HHS to involve prisoners, the following two actions must occur:

- ⇒ The Institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305.
- ⇒ The Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

To fulfill these requirements, the IRB Staff will prepare and send to OHRP a certification letter stating:

- ⇒ The IRB (including name and address) has been constituted according to the regulations;
- ⇒ The IRB considered and made the required 7 findings set forth in 45 CFR 46.305;
- ⇒ The category of approval under 45 CFR 46.306 that permits this research to go forward with prisoners as human subjects;
- ⇒ Whether OHRP needs to consult with appropriate experts and publish a Federal Register Notice.

The certification letter will specifically identify the research protocol and any relevant HHS grant application or protocol. A copy of the research proposal, including the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms, and any other information requested by the IRB during initial IRB review, will be sent with the letter.

OHRP will determine which permissible category, if any, under which the proposed research qualifies. OHRP is responsible for consulting with experts and/or publishing in the Federal Register as appropriate with respect to paragraphs (iii) and (iv) of 45 CFR 46.306(a)(2).

Enrollment of prisoners into a DHHS conducted or supported research study may not begin until OHRP issues its approval in writing to the institution of behalf of the Secretary.

Participant becoming prisoner during research

If a research participant becomes a prisoner after enrollment in a research study, the Principal Investigator is responsible for notifying the IRB immediately. If the research proposal was not reviewed and approved by the IRB in accordance with the HHS regulations at 45 CFR 46, Subpart C, the PI must stop all research interactions with the participant, including obtaining identifiable private information, until the requirements of Subpart C have been satisfied by the IRB. OHRP allows one exception as follows: "In special circumstances in which the principal investigator asserts that it is in the best interest of the subject to remain in the research study while incarcerated, the IRB Chairperson may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied."

IRB Records

The IRB will prepare and maintain adequate documentation of IRB activities regarding research involving prisoners. That documentation will include, but is not limited to, the curriculum vitae of the prisoner or prisoner representative serving on the IRB, a record of the determination of the IRB regarding the seven additional findings required under HHS regulations at 45 CFR 46.305(a) and copies of all correspondence with OHRP.

Additional Requirements

In addition to IRB approval, investigators must obtain approval of the TDOC.

Tennessee Department of Corrections (TDOC) policy number 114.02 outlines the procedures for acquiring research approval within the department. These "Submittal instructions for research applicants" outline the guidelines as established by policy [114.02 (VI)(C)(1) for proposing and conducting research within TDOC facilities. The research process within the TDOC is consistent with American Correctional Association (ACA) standards referenced in *Standards for Adults Correctional Institutions, third edition*. Specific ACA standards pertaining to research activities within the Department of Correction include 3-4105, 3-4106, 3-4107, 3-4108, 3-4109, 3-4110 and 3-4373.

Because of this law, the IRB must ensure that all appropriate approvals are obtained.

Under 28 CFR 512, the Federal Bureau of Prisons places special restriction on research that takes place within the Bureau of Prisons. Additional requirements for prospective researchers to obtain approval to conduct research within the Federal Bureau are outlined.

Prisoners Who Are Minors

When a prisoner is also a minor (e.g., an adolescent detained in a juvenile detention facility as a prisoner) the special protections regarding children in research will also apply.

Recruitment and Selection of Participants

Research Advertising Materials Guidelines

It is the policy of both the ETSU IRB and the ETSU/VA IRB that non-coercive methods must be used by investigators to recruit subjects. Procedures for enrolling subjects and compensation for subjects must minimize the possibility of coercion or undue influence. Direct advertising for research participants is considered to be the start of the informed consent and participant selection process.

For VA Studies: Non-veterans may be entered into VA approved research studies only when there are insufficient veterans available to complete the study. All regulations pertaining to the participation of veterans as research subjects pertain to non-veterans subjects enrolled in VA-approved research.

In VA studies, during the recruitment process, researchers must take initial contacts with veterans in person and/or by letter prior to any telephone contact and provide a telephone number or other means that veterans can use to verify the validity of the study (one source of information about clinical trials is <http://www.clinicaltrials.gov>). After recruitment and during the follow-up phase, VA researchers should begin phone calls by referring to previous contacts and the information provided on the informed consent document.

In addition, for VA studies, researchers must restrict their telephone and other contacts with veterans to only those procedures and data elements outlined in IRB-approved protocols. In these contacts researchers must not request social security numbers.

All advertisements, questionnaires, surveys, testing forms and/or introduction letters associated with the study and intended for subject use or view must be submitted to the IRB for approval.

Advertisements may not include the following:

- ⇒ The ad cannot state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- ⇒ The ad cannot make claims, either explicitly or implicitly, that the drug, biologic, or device is safe or effective for the purposes under investigation.
- ⇒ The ad cannot make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, or device.
- ⇒ The ad cannot use terms such as “new treatment,” “new medication,” or “new drug” without explaining that the test article is investigational.
- ⇒ The ad cannot promise free medical treatment when the intent is only to say participants will not be charged for taking part in the investigation.
- ⇒ The ad cannot include any exculpatory language

Advertisements to recruit participants should be limited to the information that prospective participants need to determine their eligibility and interest. When appropriately worded, the following items should be included in advertisements:

- ⇒ name and address of the Investigator;
- ⇒ purpose of the research;
- ⇒ criteria to be used to determine eligibility in a summary form;
- ⇒ location of the research (e.g., Vanderbilt);
- ⇒ a brief description of the study activities, when appropriate;
- ⇒ potential benefits, if any; and
- ⇒ name and phone number of the person to contact for further information.

Advertisements may also include a statement that participants will be paid, but should not emphasize the payment of the amount to be paid, by such means as larger or bold type.

The material should clearly state, "This is a Research Study," or, when appropriate, "This Research Study involves the use of an Investigational Drug or Device."

IRB Review

The IRB Chair, or his/her designee, may approve advertisements that are easily compared to the approved Informed Consent document through the expedited mechanism. If the reviewer has any doubt or there are any complicating issues involved, the convened board should review the advertising.

The IRB will review the information contained in the advertisement and its method of communication to determine that participants are not coerced.

The IRB must review the final copy of all advertisements, including print advertisements and audio/video tape for broadcast. If an advertisement is to be broadcast, the IRB may review and approve the wording prior to taping. The approval of the final taped message prepared from the IRB-approved text can be given through expedited review.

Payment of Participants

Payment to research participants is not considered a benefit but a recruitment incentive. The amount and schedule of all payments should be described in the IRB application at the time of initial review, including the amount of payment, and the proposed method and timing of disbursement. The IRB must review this information to assure that the amount, method, or timing of payment are not coercive and do not present undue influence. Credit for payment should accrue as the study progresses and not be contingent upon the participant completing the entire study. While the entire payment should not be dependent upon completion of the entire study, payment of a small proportion as an incentive for completion is acceptable, providing that such incentive is not coercive. The IRB should determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.

Procedures for prorating payment should the participant withdraw should be considered when submitting the IRB application and informed consent documents. Unless it creates undue inconvenience or a coercive practice, payment to participants who withdraw from the study may be paid at the time the study would have been completed had they not withdrawn. For example, in a study lasting only a few days, it may be permissible to allow a single payment date at the end of the study, even to participants who withdraw before completion.

All information concerning payment, including the amount and schedule of payment(s), should be set forth in the informed consent document and the narrative

Compensation for participation in a trial offered by a sponsor may not include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

For VA Studies: VA policy prohibits paying human subjects to participate in research when the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual medical care.

Payment may be permitted, with IRB approval, in specific circumstances outlined in IRB Policies.

Emergency Use

Emergency use is defined as the use of a test article (e.g., investigation drug, device or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use. The investigator is still required to obtain consent under these circumstances. The FDA exempts from IRB review the emergency use of a test article so long as the emergency use is reported to the IRB within five working days of its occurrence. Any subsequent use of the test article is subject to IRB review [21 CFR 50.23; 21 CFR 56.104(c)]. When emergency care involves investigational drugs, devices, or biologics, FDA requirements must be satisfied.

Emergency Use

When an investigator identifies a need for emergency use of a test article, the following procedures must be implemented:

⇒ The IRB Chair or Vice Chair, or in their absence, a physician member of the IRB should be contacted. If the Chair is not an M.D., the Chair will make immediate contact with a qualified physician who is either 1) a member of the IRB, or 2) referred to the Chair by the member-physician as a qualified consulting-physician for concurrence on the emergency use approval. When the IRB Chair or Director receives a request for emergency use from a clinical investigator, the IRB Chair will examine each case, receive a collaborating statement from a physician associated with neither the patient nor the current attending physician (consult) supporting the emergency use and, upon request, assure the institution that the emergency use was justified. A copy of the FDA 1572 and approved IND or IDE will be requested of the investigator.

The ETSU/VA IRB Chair will also determine if the research is (or was) not a systematic investigation designed to develop or contribute to generalizable knowledge. The Chair will also determine that unless the criteria for the exception to the requirement for consent are (were) met, consent will be (or was) sought from each prospective participant or the participant's legally authorized representative, in accordance with and to the extent required by FDA regulations and will be appropriately documented, in accordance with and to the extent required by FDA regulations.

⇒ The investigator must report the emergency use of the test article to the IRB within five (5) working days. The ETSU/VA IRB Chair reviews this report and determines whether the circumstances of the emergency use complied with regulatory requirements.

Subsequent Use

Any subsequent use of the test article is subject to full IRB review. Subsequent use means any use of the test article that occurs after its initial emergency use. Should the investigator or IRB anticipate a subsequent need to use the test article, a complete formal application must be made for IRB review at a convened meeting.

Emergencies for which Informed Consent is not Feasible

In some emergency circumstances, it may not be feasible to obtain informed consent prior to using the test article. The regulations [21 CFR 50.23(a)(1-4) and (b-c)], [.116(d)(3)]

and.116(d)(4)(f)], therefore provide an exception for informed consent requirements for such situations. Except as stated below, in order for the exception to apply, both the investigator and a physician who is not otherwise participating in the clinical investigation must certify in writing all of the following:

- ⇒ the subject is confronted by a life-threatening situation necessitating use of the test article;
- ⇒ the subject is unable to provide effective consent;
- ⇒ there is insufficient time in which to obtain consent from the subject's legal representative; and
- ⇒ there is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is necessary to save the life of the subject and there is insufficient time to obtain the independent certification required before using the test article, the investigator is to make his or her own written determinations, and within five (5) working days after the use of the test article, obtain the written review and evaluation of a physician who is not participating in the clinical investigation.

Documentation, in both instances, must be submitted to the IRB Coordinator within (5) working days after the use of the test article. The ETSU/VA IRB Chair reviews this report and determines whether the use of the exception for informed consent requirements complied with regulatory requirements.

Each primary affiliated hospital associated with this institution has a designated person for contact for emergency use.

Device

An Significant Risk (SR) device study is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. An NSR device investigation is one that does not meet the definition for a significant risk study.

Non-Significant Risk (NSR) device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56] to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].

In reviewing studies involving medical devices, the Medical Campus ETSU/VA IRB will make two determinations:

- (1) whether a device study represents a significant or non-significant risk; and
- (2) whether the study should be approved.

These questions will be considered separately because the issues involved in making these decisions are quite different. Determining whether a device study poses a significant risk will be based solely on considerations of risk to subjects, while IRB approval of the study is based on many factors.

The initial assessment of whether or not a device study presents a non-significant risk (NSR) is made by the sponsor.

In addition to receiving a completed Form 103, narrative, informed consent, protocol and investigator's brochure (if available), the IRB must receive a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The IRB must also be informed whether other IRBs have reviewed the proposed study, and what determinations were made. In addition, the IRB must be informed of the FDA's assessment of the device's risk if such an assessment has been made. If the sponsor considers that a study is NSR, the sponsor must provide the IRB an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. The sponsor must provide the IRB with a risk assessment and the rationale used in making its risk determination [21 CFR 812.150(b)(10)].

For any device protocol considered (by FDA) to present significant risk, an IDE number will be required prior to submission to the ETSU/VA IRB for initial review. Conversely, if the FDA has made a determination of non-significant risk, than a copy of the determination letter received from FDA should be submitted with the protocol. The IRB may also consult with FDA for its opinion. The IRB uses its expertise, information in the FDA regulations and guidelines, and the risk evaluation provided in the application to determine the risk category.

The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA.

If the IRB disagrees and determines that the device is SR, the IRB informs the investigator and the sponsor in writing of this decision and its basis. The sponsor should notify FDA that an SR determination has been made. If the IRB determines that a device study is SR, the study **may not** begin until both the IRB and FDA approve the investigation. The study can be conducted as an SR investigation following FDA approval of an IDE application.

The risk determination should be based on the proposed use of a device in a investigation, and not on the device alone. In deciding if a study poses an SR, the IRB considers the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the participant must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB considers the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

FDA has the ultimate decision in determining if a device study is SR or NSR.

If the IRB decides the study is Significant Risk,

- ⇒ The IRB Coordinator forwards a letter to notify the sponsor and investigator of the decision that the study is significant risk.
- ⇒ The IRB tables the study until an IDE is obtained by the sponsor.
- ⇒ After IDE is obtained and submitted, the convened IRB reviews the study.

If the IRB decides the study is Non-Significant Risk,

- ⇒ IRB proceeds to review study applying requisite criteria [21 CFR 56.111]

Minutes of IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

If the investigator or organization is acting as the sponsor, the investigator or sponsor must follow all the additional regulatory requirements of sponsors. The IRB must evaluate whether the investigator knows how to follow the additional regulatory requirements of sponsors. In order to determine this evaluation, the IRB requires any investigator acting as the sponsor to read the FDA's "Responsibilities for Sponsors of Significant Risk Device Studies, Responsibilities for Sponsors of Non-Significant Risk Device Studies" , "Responsibilities for Investigators of Significant Risk Device Studies, Responsibilities for Investigators of Non-Significant Risk Device Studies" published on-line at <http://www.fda.gov/cdrh/devadvice/ide/print/responsibilities.html>. The IRB receives an signed attestation that the investigator/sponsor has read this document prior to issuing final study approval.

Reporting of Unanticipated Problems/Events

I. Pertinent Definitions:

Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO): Includes those events that (1) are not expected given the nature of the research procedures and the subject population being studied (2) suggest that the research places subjects or others at a greater risk of harm or discomfort related to the research than was previously known or recognized and (3) are related or possibly related to the research.

Possibly related: there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research

Unexpected: unexpected in terms of nature, severity or frequency given the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document and given the characteristics of the subject population being studied

Serious Adverse Event: any adverse event that results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

For VA studies, an adverse event or problem in research is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent the outcomes above or to prevent substantive harm or damage (or risk of substantive harm or damage) to the safety, rights, or welfare of research subjects, research staff, or others.

Unexpected Adverse Event: As defined by the FDA, any adverse event, the specificity or severity of which is not consistent with the current Investigator Brochure; or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the Investigator Brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the Investigator Brochure only listed cerebral vascular accidents. **Clarification Note:** “Unexpected,” as used in this definition, refers to an adverse event that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product and not listed in the Investigator’s Brochure.

Unexpected adverse event: any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is NOT consistent with either (1) the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved consent document and (b) other relevant sources of information, such as product labeling and package inserts; or (2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

II. Summary Policy

Federal regulations require the organization to ensure prompt reporting of “any unanticipated problems involving risk to subjects or others” to the IRB, regulatory agencies, and institutional officials.

For non-VA studies, the ETSU/VA and ETSU IRB require investigators to promptly submit any problem or event that meets the following criteria to the IRB within 10 working days using the Form 109 (unanticipated problem report) signed by the PI.

For VA studies, VA reporting requirements require immediate reporting of the loss or theft of VA research data/information or portable media such as laptops or personal computers- see Section III. VA reporting requirements require Investigators, VA Research Compliance Officers, and other members of the VA research community to report all problems involving, or suggesting, risks to subjects or others in VA Research to the Associate Chief of Staff for Research (ACOS for R) and the ETSU/VA IRB as soon as possible but no later than five business days after becoming aware of the problem.

Events to be reported include:

- a. any event, including on-site and off-site adverse events, injuries, side effects, deaths, or other problems, which in the opinion of the local PI, was unexpected, , suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized , and was related to or possibly related to the research.*
- b. Any accidental or unintentional change to the IRB-approved protocol that involves risks or has the potential to recur
- c. Any deviation from the protocol taken without IRB approval to eliminate apparent immediate hazard to a research participant
- d. Any publication in the literature, safety monitoring report,(including Data and Safety Monitoring Reports), interim result, or other finding that indicates an unexpected change to the risk/benefit ratio of the research.
- e. Any breach in confidentiality that may involve risk to the participant or others
- f. Any complaint of a participant that indicates an unanticipated risk or that cannot be resolved by the research staff
- g. any local death, whether anticipated or not
- h. incarceration of a participant
- i. Any other possibly related event which in the opinion of the investigator constitutes an unanticipated risk.
- j. Addition of a black box warning on any drug used in your research (for VA studies, this also includes VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to a VA research study
- k. interruptions of subject enrollment or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff. or others.
- l. Any work-related injury to personnel involved in human research, or any research-related injury to any other person, requiring more than minor medical intervention or that leads to serious complication or death.
- m. Any Data Monitoring Committee (DMC) report or any sponsor analysis describing a safety problem

- n. For VA studies, any local Serious Adverse Event (see definition)
- o. For VA studies, any problem that involves or suggests risks to VA research subjects or anyone else in VA research.

III. Non-VA PI Responsibilities regarding Adverse Event Assessment (category a above) SEE SECTION IV for VA studies

A. Internal adverse events

Upon becoming aware of an internal adverse event, PIs are required to promptly assess the event and determine whether the event is a UPIRTSO. PIs must evaluate each event by the following three criteria in order to make that determination.

If the answer to the three following questions is “yes”, then the event is a UPIRTSO and must be submitted to the IRB within 10 working days using the Form 109.

1. Is the adverse event unexpected?
2. Is the adverse event related or possibly related to participation in the research?

Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized? *

*Note: If the adverse event is serious (see definition above), the answer to this question is always “yes”.

If the answer to all three questions is “yes” then the event meets the definition of a UPIRTSO and must be reported to the IRB within 10 working days on a form 109 and a modification request. The modification request must outline the necessary revisions to the IRB approved protocol, consent document or other associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

If all three questions are not answered “yes”, then the event does not meet the definition of a UPIRTSO. The event is not required to be reported to the IRB within 10 days but is reportable to the IRB in summary format at the time of continuing review.

Regardless of the determination, PIs also are responsible for ensuring that the adverse event is reported to the monitoring entity if required under the monitoring provisions described in the IRB-approved protocol or by institutional policy.

B. External adverse events

When PIs receive a report of an external adverse event, PIs are required to promptly assess the event and determine whether the event is a UPIRTSO. Only external adverse events that are identified as meeting the three criteria above must be reported promptly to the IRB as UPIRTSOs. If all three questions are not answered “yes”, then the event does not meet the definition of a UPIRTSO. The event is not required to be reported to the IRB within 10 days but is reportable to the IRB in summary format at the time of continuing review. If all three questions are answered

“yes”, then the PI must within 10 days submit BOTH a form 109 and a modification request. The modification request must outline the necessary revisions to the IRB approved protocol, consent document or other associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

Reports of off-site events occurring in studies that are completed and closed at the local site should be reported if the event meets the IRB definition as detailed above AND the local PI judges that this event may affect risk to participants who have completed the study.

Follow-up reports of an off-site event may be submitted on a tracking log without an accompanying Form 109 if the following are true:

- the initial report of the event was submitted as a UPIRTSO on a Form 109
- the local PI has determined that the follow-up information does not contribute meaningful new information

All problems/events that do not meet these criteria should be reported to the IRB in summary form (table or spreadsheet) at the time of continuing review.

IV. VA PI Responsibilities regarding Adverse Event Assessment (category a above)

A. Internal adverse events

Upon becoming aware of an internal adverse event, PIs are required to promptly assess the event and make 2 determinations.

1. Is the event a local SAE? (see definition in Section I)

If the event is a local SAE, the PI must report the event to the ACOS for R and the ETSU/VA IRB using form 109 as soon as possible, but no later than 5 business days after the event has become known to the investigator.

2.If the event is not a local SAE, the PI must evaluate each event by the following three criteria in order to determine whether the event is a UPIRTSO.

If the answer to the three following questions is “yes”, then the event is a UPIRTSO and must be submitted to the IRB within 5 business days using the Form 109 and a modification request. The modification request must outline the necessary revisions to the IRB approved protocol, consent document or other associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

1. Is the adverse event unexpected?
2. Is the adverse event related or possibly related to participation in the research?
3. Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized?

If all three questions are not answered “yes”, then the event does not meet the definition of a UPIRTSO. The event is not required to be reported to the IRB within 5 days but is reportable to

the IRB in summary format at the time of continuing review. Regardless of the determination, PIs also are responsible for ensuring that the adverse event is reported to the monitoring entity if required under the monitoring provisions described in the IRB-approved protocol or by institutional policy.

B. External adverse events

When PIs receive a report of an external adverse event, PIs are required to promptly assess the event and determine whether the event is a UPIRTSO. Only external adverse events that are identified as meeting the three criteria above must be reported promptly to the IRB as UPIRTSOs. If all three questions are not answered “yes”, then the event does not meet the definition of a UPIRTSO. The event is not required to be reported to the IRB within 5 days but is reportable to the IRB in summary format at the time of continuing review. If all three questions are answered “yes”, then the PI must within 5 business days submit BOTH a form 109 and a modification request. The modification request must outline the necessary revisions to the IRB approved protocol, consent document or other associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study.

Reports of off-site events occurring in studies that are completed and closed at the local site should be reported if the event meets the IRB definition as detailed above AND the local PI judges that this event may affect risk to participants who have completed the study.

Follow-up reports of an off-site event may be submitted on a tracking log without an accompanying Form 109 if the following are true:

- the initial report of the event was submitted as a UPIRTSO on a Form 109
- the local PI has determined that the follow-up information does not contribute meaningful new information

All problems/events that do not meet these criteria should be reported to the IRB in summary form (table or spreadsheet) at the time of continuing review.

V. *VA Reporting of Loss or Theft of VA research data/information

The loss or theft of VA research data/information or portable media such as laptops or personal computers must be immediately reported (as soon as it is discovered that there has been a loss) as follows:

Report the loss to security/ police officers IMMEDIATELY. If within a VA health care facility, notify the VA police. If the loss or theft occurs while on travel or at another institution, notify the security police officers at the institution (such as hotel security, university security, etc.) as well as the police in the jurisdiction where the event occurred.

Obtain the case number and the name and badge number of the investigating officer. If possible, a copy of the case report should be obtained.

Report the incident IMMEDIATELY to your immediate supervisor*

VA Privacy Officer at your facility *

VA Information Security Officer at your facility*

ACOS at your facility*

Report the incident to the IRB using a Form 109 (Unanticipated Problem Involving Risks to Subjects or Others).

* The name and contact information should always be readily available. Wallet cards that list the contact name and number of the James H. Quillen VA ACOS, the VAMC Privacy Officer and the VAMC Information Security Officer are available through the VA R&D office and the IRB Office.

VI. IRB Responsibilities

The IRB Coordinator will present the written report of the unanticipated event received from the investigator to the IRB Chair within 5 days.* (SEE EXCEPTION BELOW FOR VA STUDIES). The Chair will perform an initial review, and determine whether the event is an unanticipated problem involving risks to participants or others. In addition, for VA studies, the Chair will determine and document on the UPIRTSO Reviewer Form whether the problem or local SAE is serious, unanticipated, or related or possibly related. The Chair determines the action required based on his/her decision. If the Chair determines that the event is not a UPIRTSO, no further action is taken. If the Chair determines that the event is a UPIRTSO, the Chair will consider suspension or other immediate action such as notification of participants and refer the report to the IRB. If the Chair determines that there is the potential of immediate harm to participants, the Chair may immediately suspend the study pending the IRB's receipt and review of the unanticipated problem and determination of any required actions.

If Chair determines that the report is a UPIRTSO, the report, with any attached documents, the narrative description of the project, and the current approved informed consent, will be forwarded to the IRB Primary Unanticipated Problem (UP) Reviewer for initial review. The UP Reviewer, appointed by the IRB, will review all UPIRTSOs submitted and report findings and any recommendations for local ICD revisions to the IRB. In addition, all IRB members receive a copy of the Unanticipated Event Form (Form 109), the narrative description of the project, and the currently approved consent document. If additional information is required in order to make a final determination concerning the event, the investigator will receive such a request in writing from the Chair/Board. The report will be added to the next agenda for the convened board. VA events requiring review by the convened board must be reviewed at the IRB's next convened meeting. Refer to Policy 34 for VA reporting requirements.

Examples of corrective actions or substantive changes that might need to be considered by the IRB in response to a UPIRTSO include:

- a. Modification of inclusion or exclusion criteria to mitigate the newly identified risk
- b. Implementation of additional procedures for monitoring subjects
- c. Suspension of enrollment of new subjects
- d. Suspension of research procedures in currently enrolled subjects
- e. Modification of informed consent documents to include a description of newly recognized risks
- f. Provision of additional information about newly recognized risks to previously enrolled subjects (if IRB determines that an informed consent modification is warranted, the convened IRB must determine and document in the minutes whether or not previously enrolled subjects must be notified of the modification and if so, when such modification must take place and how such notification must be documented)
- g. Reconsideration of study approval

h. Revision of the continuing review timetable

i. Requirement of notification of past participants

The IRB may deem it necessary to directly audit the research site and medical records pertaining to the event, monitor the consent process, interview participants or witnesses, or suspend/withdraw IRB approval until such time that the safety of the participants can be assured. If information that may relate to subject's willingness to continue to take part in the research is noted, the IRB will require notification of current participants. The IRB may require that current participants be re-consented. The IRB may terminate the research.

Correspondence will be forwarded to the Principal Investigator as per the decision of the IRB following the completion of the review process.

If the Chair determines the event is a UPIRTSO, the reporting requirements outlined in Policy 34 will be followed.

The ETSU/VA IRB Chair is responsible for reviewing any report of a local death to determine if the death is unanticipated. For VA studies, if the Chair determines that the death is unanticipated, the ETSU/VA IRB Coordinator immediately forwards the Chair's written assessment to the VA AO. The VA AO is responsible for submitting the report to ORO within 24 hours of the Chair's determination that the death was unanticipated.

If the local site submits a tracking log for non-reportable events to satisfy sponsor requirements, the events/problems listed on the tracking log will be acknowledged by the IRB Chair, as indicated by his/her initials and date in the final column of the tracking log. A copy of the log will be filed with the study file, and the original returned to the investigator.

*For VA studies,

If the IRB receives a report of a reported loss or theft of VA research data/information or portable media, the report will be immediately forwarded to the HRPP Director. The HRPP Director will immediately follow the reporting pathway outlined in Section III above.

References

45 CFR 46. 103(b)(4)(iii)

21 CFR 56.108(b)(1)

OHRP Compliance

45 CFR 46 104(a)

45 CFR 35 104 (b)

VHA Handbook 1058.1

Appendix A, Memo from Deputy Under Secretary for Health Operations and Management (DUSHOM) and Chief Research and Development Officer (CRADO) dated February 6, 2007

OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events dated January 15, 2007

VHA Handbook 1058.01 February 27, 2009

Performance Sites

Definitions

A. Engaged: An institution becomes "engaged" in human subjects research when its employees or agents¹ (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [\[45 CFR 46.102\(d\),\(f\)\]](#).

An 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.

It is the policy of both the East Tennessee State University Campus Institutional Review Board (ETSU IRB) and the East Tennessee State University/ Veterans Affairs Institutional Review Board (ETSU/VA IRB) that appropriate approvals for "engaged" and "non-engaged" performance sites are obtained and documented.

The PI will obtain and submit appropriate documentation of IRB or institutional approval as required and will notify the IRB of site closures as they occur. The IRB Coordinator will verify that the appropriate documentation for performance sites has been submitted to the IRB before final approval is issued. The IRB Coordinator will verify the FWA and IRB registration number for performance sites in category 1.

IRB reviewers verify the determination of "engaged" versus "non-engaged."

Performance Site Category	Description	FWA required?	Required approval
Category 1	engaged in re- search with federal re- search sup- port or direct award for study	Yes	Submit copy of site IRB approval or re- quest that ETSU IRB be IRB of Record.
Category 2	engaged in re- search with no federal research sup- port or direct award for study	No	Submit copy of site IRB approval or re- quest that ETSU IRB be IRB of Record.
Category 3	Performance site not engaged in research with established IRB	No	Submit copy of site IRB approval or re- quest that ETSU IRB be IRB of Record.
Category 4	Performance site not engaged in research without estab- lished IRB	No	Submit letter of permis- sion from the appropri- ate institutional official stating that the re- search may be con- ducted at site.

Deception Research

It is the policy of both the East Tennessee State University Campus Institutional Review Board (ETSU IRB) and the East Tennessee State University/ Veterans Affairs Institutional Review Board (ETSU/VA IRB) that the basic principles outlined in the Belmont Report (respect for participants, beneficence, and justice) guide the ethical conduct of research. When investigators plan to withhold information or provide participants false information about some aspect of the research, the proposed use of deception imposes additional responsibilities on the investigator and the IRB.

Criteria

The federal regulations do not allow the IRB to approve a study involving deception if that study does not meet the criteria for granting a waiver or alteration of the requirement for informed consent.

Those criteria are:

1. The research involves no more than minimal risk to the subjects. (Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Note that the definition of minimal risk for prisoner at 45 CFR 46.303(d) differs from the definition of minimal risk for other research- see Policy 15)
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
3. The research could not practicably be carried out without the waiver or alteration.
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation. (Source: 45 CFR 46.116(d))
5. The research is not FDA-regulated.

In addition, the IRB requires that studies involving deception meet the following criteria:

1. Information to be withheld would not influence the decision of prospective subjects about participating in the research. (Source: OHRP IRB Guidebook, Chapter III, Section B)
2. Incomplete disclosure is truly necessary to accomplish the goals of the research. (Source: Belmont Report, April 18, 1979)
3. Investigator's plan regarding debriefing is appropriate. (Source: OHRP Guidebook, Chapter V, Section A, Behavioral Research)
4. The proposed subject population is suitable. (Source: OHRP Guidebook, Chapter V, Section A, Behavioral Research)
5. The use of deception in this research is justified by the study's significant prospective scientific, educational, or applied value. (Source: APA Ethical Principles of Psychologists and Code of Conduct)

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