IRB Policy 21: IRB Reliance Policy
Version January 7, 2020

I. Pertinent Definitions

A. **Reliance agreements** are defined as the agreement, also called an IRB authorization agreement (IAA), which documents respective authorities, roles, responsibilities, and communication between an organization providing the IRB review and a participating organization relying on a reviewing IRB.
B. **Reviewing IRB** is the IRB responsible for review and oversight of a research project. Also known as the IRB of record or the sIRB.
C. **Relying Institution** is an institution that agrees to accept IRB review and oversight from a reviewing IRB.
D. **Multi-site** means that the same research procedures (i.e., protocol) are being used to conduct non-exempt human subject research at more than one domestic site.
E. **Lead or coordinating site** is the site that (usually) receives the grant or contract and establishes subawards or subcontracts with participating sites.
F. **Participating site** in a multi-site study is a domestic entity that will rely on the sIRB to carry out the site's IRB review of human subject research for the multi-site study.
G. **Lead PI** is the PI in whose name the overall grant application was submitted to the sponsor and who is responsible for the overall management, supervision, and coordination of the study across all participating sites, including the sIRB requirements.
H. **sIRB**, or Single IRB, is the IRB of record, selected on a study-by-study basis, that conducts the IRB review for participating sites of the multi-site study.
I. **Sponsor** is any individual, company, institution, organization, or agency that takes responsibility for the initiation, management, and/or financing of research.
J. **Local context** is all of the elements specific to a local site that may affect the conduct of the research such as state and local laws and institutional policies.
K. **Local review**, or institutional review, is all of the elements of review, except IRB review, required by a relying institution to be conducted in accordance with their human research protection program, such as review of investigator training, conflict of interest, and HIPAA compliance.

II. Summary Policy

This Policy applies to the conduct of human subjects research under the jurisdiction of the ETSU Human Research Protection Program (HRPP). This includes research under the oversight of the ETSU and ETSU/VA IRBs and research for which ETSU or its affiliates are relying on an external IRB for oversight. ETSU may choose to accept the review and approval of human subject research studies as granted by an external IRB

organization, or may choose to be the reviewing IRB for other institutions. This policy includes the steps taken to ensure that the rights and welfare of human research participants are protected when ETSU relies on the services of another organization, and when ETSU chooses to be the reviewing IRB for other institutions.

The ETSU Vice Provost for Research has the ultimate authority regarding whether or not to rely on an external IRB, or whether or not the ETSU IRBs will serve as reviewing IRB for any particular study. In accordance with OHRP Guidance, when ETSU enters into a reliance agreement for cooperative research, the relationship is documented with a written agreement between the reviewing IRB and relying institution, which sets forth obligations of the IRBs and institutions in the terms of the agreement.

Examples of when reliance may be considered include: research in which ETSU has an institutional conflict of interest, multi-site research in which ETSU employees are engaged in research, industry-sponsored clinical trials, and federally sponsored research for which sIRB is required.

III. Criteria for the use of an External IRB

ETSU may rely on the IRB of another organization provided one of the following is true:

- The IRB is under the purview of an AAHRPP accredited organization

- An ETSU investigator is a collaborator on the human research protocol that is primarily conducted at another organization's site, and the investigator's role does not include interaction or intervention with subjects.

- ETSU is engaged in the human subjects research solely because it is receiving federal funds. Employees and agents of the institution do not interact or intervene with subjects, gather or possess private, identifiable data about subjects, nor obtain the consent of subjects.

For ETSU research, the designated IRB may be an independent IRB not associated with ETSU, or it may be the IRB at a research organization that agrees to serve as the IRB of record. For VA research, however, reliance on a commercial IRB is prohibited. For collaborative VA research, the reviewing IRB must be either the VHA Central Office IRB, an IRB of another VA facility, an IRB of another federal agency, or a non-affiliated IRB that has been specifically designated by ORD.

Reliance on non-accredited organizations

In some circumstances ETSU may elect to rely on the IRB of a non-accredited human research protection program to facilitate IRB review of collaborative research. Additional assurance will be required from the non-accredited reviewing IRB to ensure the highest

ethical standards for the proposed research. ETSU will not rely on a non-accredited IRB for greater than minimal risk research.

For minimal risk studies, ETSU will:

a. Obtain an assurance from the non-accredited IRB that it will conduct its review consistent with applicable ethical standards and regulations, and that it will report any regulatory violations or investigations of the reviewing IRB by regulatory agencies, such as OHRP, FDA, or regulatory agencies in other countries. Both of these elements will be included in the terms of the reliance agreement.

b. Evaluate relevant policies and procedures of the reviewing IRB to determine whether they meet ETSU standards (are similar in protection to ETSU IRB policies).

In order for ETSU to rely on an external IRB, the Vice Provost for Research (VPR) and the HRPP Director must determine that external reliance is appropriate and that the proposed IRB is acceptable. If it is determined that external reliance is not appropriate or that the proposed reviewing IRB is not acceptable, the PI is notified in writing of this decision and the rationale. The PI may choose to submit it for formal review by the ETSU or ETSU/VA IRB, if reliance on the specified external IRB is not required in order to be a participating site.

IV. ETSU as a relying site

When ETSU is relying on an external IRB, the research cannot begin until the IRB approval is obtained AND appropriate approvals/registrations are also obtained from ETSU. ETSU must authorize the use of any external IRB for each study, even under pre-established cooperative or reliance agreements. As ETSU maintains responsibility for safeguarding the rights and welfare of human subjects and complying with applicable regulation in the conduct of cooperative research, the institution will maintain a record of pertinent study records for each study in which ETSU relies on an external IRB. See Policy 30 for Record Keeping.

The designated local investigator at ETSU must initiate the process to request reliance on an external IRB by submitting the Request to Rely on an External IRB xForm. ETSU must have adequate information regarding the proposed study to make a reliance determination. Documentation from the external IRB or lead site must be submitted to facilitate the review of the reliance request, which may include the research protocol, proposed consent form(s) and HIPAA authorization(s), grant or scope of work, recruitment advertisements, relevant drug or device documentation, waiver documentation, participant documents, and a list of local key personnel and their roles. If deemed necessary by the HRPP Director, copies of relevant IRB minutes may be requested.

The HRPP Director will be the primary point of contact for all reliance requests, and in consultation with the VPR, will:

- Ensure that the proposed external IRB is appropriate and qualified
- Confirm or establish any necessary reliance agreements
- Provide the Institutional Profile to the external IRB and local context information, if required
- Confirm compliance with local laws, standards, and institutional requirements as appropriate
- Ensure all appropriate local ancillary reviews are completed
- Administratively review all subsequent external IRB registration events

If the reliance is deemed appropriate, the investigator must provide the ETSU IRB with a copy of the external IRB initial approval letter before the reliance request is approved.

The ETSU investigator is responsible for:

- Following the policies of the reviewing IRB, including submitting using their forms, following their reporting requirements, and complying with stipulations
- Providing the external IRB a copy of the fully executed reliance agreement
- Ensuring that any relevant conflicts of interest are disclosed to the reviewing IRB any COI management plans are provided to the reviewing IRB
- Obtaining any required ancillary review and approvals (i.e., Biosafety) and providing the results of these review to the reviewing IRB
- Maintaining copies of relevant research records and making them available for inspection by monitors and auditors
- Submitting documentation for continuing registration, major amendments, monitoring or audit reports, and serious adverse events, protocol violations, noncompliance, or unanticipated problems to ETSU via IRB Manager

The investigator will be provided a written ETSU External IRB Registration letter, which confirms ETSU has authorized the reliance. Subsequent external IRB registration events will be administratively reviewed by the VPR, and the PI will receive written documentation acknowledging the submission. The VPR will be responsible for reviewing and coordinating the investigation of issues of potential serious or continuing noncompliance, unanticipated problems, or research misconduct in coordination with the reviewing IRB.

If the reviewing IRB makes a determination of serious or continuing non-compliance, or suspension or termination of the study, that determination will be reported to the ETSU or ETSU/VA IRB for informational purposes. ETSU HRPP Director will notify MSHA Research Department if a MSHA study.

V. ETSU as a reviewing IRB

The ETSU IRBs may serve as the IRB of record for research sites external to ETSU under conditions defined in this Policy. Examples of when such reliance may be permitted include: multisite research in which an ETSU investigator is the lead PI, multisite research in which an ETSU investigator is a collaborator and ETSU, the VA, or MSHA are the primary data collection sites, or as part of cooperative agreements to which the ETSU IRBs have joined.

The HRPP Director, in conjunction with the IRB Chair, will consider the following to determine whether either ETSU IRB will serve as the IRB of record:

- The size, scope, and complexity of the research and number of relying external sites is reasonable in proportion to the ETSU HRPP resources to ensure adequate oversight
- An ETSU investigator has a prominent role in the multisite study
- Reliance on either ETSU IRB does not result in unreasonable liability for ETSU nor compromise the integrity of the HRPP
- The relying sites are in good standing with OHRP, FDA, and all applicable regulatory agencies

The lead ETSU investigator is responsible for communication among the ETSU IRB and the relying sites' IRB and research study teams. The lead ETSU investigator is responsible for all submissions to the ETSU IRB on behalf of the relying sites. The lead ETSU investigator must comply with all responsibilities of the PI (See Policy 3), in addition to:

- Obtaining study site information pertinent to the IRB review and providing that information to the ETSU IRB,
- Dispensing all pertinent study details and multisite safety information to the relying sites,
- Promptly collecting safety information, protocol violations, and other reportable information from the relying sites and submitting them to the ETSU IRB for review,
- Relaying questions or requests for modifications from the ETSU IRB to relying sites and submitting site responses to the ETSU IRB for review, and
- Providing IRB approval documentation to the relying sites in accordance with their IRB policy.

The ETSU IRB serving as the IRB of record will be guided by all federal regulations applicable to the research involving human subjects in its review of research conducted by relying sites. The ETSU IRB will ensure adequate review consideration for the local context of each relying site and will perform the IRB review in accordance with ETSU

IRB Policies and Procedures, which are posted publicly on the ETSU IRB website. The reviewing IRB must be able to assess sufficient information to conduct an analysis of the criteria for approval for each relying site for all applicable studies. The ETSU IRBs will ensure that convened IRB minutes pertaining to the relevant research study be made available to relying sites upon request. Responsibilities of the ETSU IRB serving as the IRB of record for external sites are further defined in the executed reliance agreement.

All communication between the ETSU IRB and each relying site should be directed through the ETSU investigator. The HRPP Director may be contacted directly by administrators at the relying site when necessary to discuss review interpretations or institutional concerns. Each relying site remains responsible for all elements of local review, except IRB review, as defined in the terms of the reliance agreement including but not limited to assessing resources, investigator credentialing, and conflict of interest review. Each relying site must:

- Ensure that its researchers participating in the research are in good standing with the site and must ensure they have met the human subjects training requirements of that site.
- Provide the ETSU IRB any relevant local context issues to be considered in the review of the proposed study.
- Provide the ETSU IRB any site specific consent form and HIPAA authorization language that must be incorporated into the approved consent form(s).
- Have processes in place to promptly report safety events, compliance concerns, legal claims, or local context issues that arise during the course of the study.
- Remain in good standing with federal agencies and have an active FWA for the duration of the reliance agreement.

ETSU will provide written documentation of the review determination to the investigator, and if applicable, the relying institution consistent with any reliance agreement.

VI. Reliance Documentation

The respective roles and responsibilities of both organizations (relying and reviewing) must be formalized in a written agreement. The written agreement must be approved and signed by the signatory official (Vice Provost for Research) at ETSU and by the correlative officials of each of the other cooperating institutions.

Reliance agreements must describe which organization (the one conducting the IRB review or the relying organization) is responsible for:

a) Providing education to researchers and confirming investigators are both qualified and credentialed to conduct the proposed research
b) Verifying appropriate resources at each participating site

c) Conducting scientific review
d) Ensuring concordance between any applicable grant and the IRB application.
e) Reviewing or investigating allegations of non-compliance, including complaints, protocol deviations, and results of audits or monitoring
f) Reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB approval. Reporting may be done by the reviewing IRB, the relying organization, or jointly, but must be clearly defined in policies or a written agreement.
g) Obtaining management plans for researcher conflicts of interest and providing those to the IRB in a timely manner prior for review by the IRB
h) Managing organizational conflict of interest related to the research
i) Reviewing and documenting HIPAA issues or serving as privacy board
j) ensuring that, should termination of a reliance agreement occur, one of the parties clearly is responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the studies

The reliance agreement terms may include additional information as appropriate for the oversight of any particular study. Expectations for relying organizations to follow the reporting policies of the reviewing IRB must be described in the written agreement. For NIH studies, the agreement must describe who is responsible for meeting additional certification requirements, such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.

Each agreement will be retained by the Office for the Protection of Human Research Subjects at East Tennessee State University for at least six (6) years past completion of the related research project. Although the agreement does not have to be sent to OHRP for initial approval, it will be provided upon written request.

VII. Continuing Review

As required, continuing review of approved research will be initiated by the IRB of Record, who shall remain responsible for determining the frequency and extent of continuing review for each study as adequate to ensure the continued protection of the rights and welfare of research subjects. The period of continuing review shall not exceed twelve months from the date of IRB approval. The PI must submit documentation of this substantive review and outcome, as conducted by the IRB of record.

References:

VHA Handbook 1200.5
Considerations Document: CITI Use of Central IRBs in Multicenter Clinical Trials
FDA Information Sheet, Non-Local IRB Review (1998)
OHRP Guidance, IRB Knowledge of Local Research Context, August 27, 2998 (updated July 21, 2000)

45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45 CFR 46.109(d), 45 CFR 46.114,
21 CFR 56.109(e), 21 CFR 56.114
NIH: Policy on the Use of a Single Institutional Review Board for Multi-Site Research (June 20, 2016)ETSU IRB Policy 10
FDA Guidance for Industry: Using A Centralized IRB Review Process in Multicenter Clinical Trials, March 2006
21 CFR 312.53 (Investigational New Drug Application 2016), Form FDA 1572 attestations, 21 CFR 812.43(c)(4)(i) (Investigational Device Exemptions 2016)
Determination of Exception to the Required Use of a Single IRB for Certain HHS Cooperative Research that is Subject to the 2018 Requirements

Related resources:
IRB Policy 21a: External IRB Procedure
IRB Policy 21 b: ETSU as Reviewing IRB