IRB Policy 24: HRPP QUALITY ASSURANCE AND QUALITY IMPROVEMENT
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I. Introduction

The ETSU Quality Assurance Process evaluates whether policies and procedures are being followed by the organization. The auditing process is conducted in order to 1) insure that investigators are conducting ethical research by using IRB approved protocols and are obtaining appropriate informed consent from the participants enrolled in their studies, 2) assure program quality, and 3) promote continuing education. Focusing mainly on the investigator research records and corresponding IRB files, the program seeks to promote institutional research within the current framework of legal, ethical, regulatory and institutional policies.

The ETSU Quality Improvement Process is implemented through a continuous cycle of assessment, development and implementation of an improvement plan, and evaluation of effectiveness.

II. Internal Compliance Reviews

Internal compliance reviews are designed to assess compliance with regulatory requirements and to continually improve IRB processes. Responsibilities for internal compliance reviews are as follows:

A. Performance Group (PG)

The IRB Performance Group consists of the ETSU IRB Chair and Vice Chair, the ETSU/VA IRB Chair and Vice-Chair, the Coordinators of both IRBs, the IRB Secretary, and the Director of the Office for the Protection of Human Research Subjects. This committee meets semi-annually.

The responsibilities of this group include:

a. Annually review IRB Policies and Procedures for compliance with all applicable regulatory requirements
b. Recommend changes to IRB Policies and Procedures to the ETSU and ETSU/VA IRB
c. Semi-annually review results of quarterly review of IRB minutes and identify any needed improvements
d. Semi-annually review results of IRB TImeline report compiled by IRB Staff

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e. Annually review the compliance education and other required records for IRB members and IRB staff
f. Annually review the results of the IRB Reporting Log
g. Annually review the ETSU and ETSU/VA IRB membership and composition for compliance with applicable policies and regulations

The focus of this group will be to evaluate compliance with applicable regulations and to evaluate IRB processes, determine an action plan, and evaluate the effectiveness of that plan.

B. Director, Office for the Protection of Human Research Subjects

Responsibilities include:

a. Review IRB submission and review template forms on an ongoing basis for compliance with policies
b. Incorporate revisions into IRB Policies and Procedures as determined by the IRB PG
c. Ensure revised IRB Policies and Procedures are disseminated to ETSU and ETSU/VA IRB members for review
d. Maintain documentation of IRB staff education on an ongoing basis
e. Maintain IRB Reporting Log documenting reporting of UPIRTSOS, serious and/or continuing non-compliance, and suspensions/terminations as required by IRB Policy 34
f. Identify and disseminate new information from FDA, OHRP and other regulatory agencies as appropriate to IRB members
g. Compile IRB Timeline Report on semi-annual basis and add to next agenda of IRB PG. The Timeline Report will include, but is not limited to:
    - mean time from complete submission of modification (both minor and non-minor) to date of IRB response letter. Target time for minor modification requests is IRB response letter within 14 days of receipt of complete modification request. Target time for non-minor (as determined by IRB Chair/ Vice-Chair) modification requests is IRB response letter within 4-6 weeks of complete modification request (sample size: minimum 20%).
    - Mean time from complete submission of an initial expedited study to date of IRB response letter. Target time is an IRB response letter within the most recent AAHRPP benchmark of complete submission of an initial expedited study (sample size: minimum 20%)
    - Mean time from complete submission of a request for exemption to date of IRB response letter. Target time is an IRB response letter within the most recent AAHRPP benchmark of complete submission of a request for exemption (sample size: minimum 20%).

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h. Generate agenda for each meeting of the IRB Performance Group, including items as identified in Section A
i. After approval by both IRB Chairs, forward summary report of PG meeting to both ETSU and ETSU/VA IRB
j. OPHRS Director reviews the completed Performance Self-Evaluation (Form 114) forms completed by IRB members for identification of continuing education topics.
k. Evaluate IRB Staff each March. The ETSU Professional Non-Faculty/Administrative Personnel Appraisal Form is completed by the Director for performance evaluation of IRB Coordinators and by the Vice-Provost for Research for evaluation of the OPHRS Director. The ETSU Classified Personnel Performance Review Form is completed by the Director for performance evaluation of the IRB Secretary. The evaluation is confidentially discussed with the employee emphasizing strong and weak points in job performance. Mutual goals are set for the employee to reach before the next performance evaluation.

C. IRB Coordinators

Coordinator responsibilities include:

a. On a quarterly basis, the ETSU IRB Coordinator will conduct a review of the most recent ETSU/VA IRB minutes by completing Form 144, Checklist for Minutes. The completed Form 144 will be forwarded to the Director.
b. On a quarterly basis, the ETSU/VA IRB Coordinator will conduct a review of the most recent ETSU IRB minutes by completing Form 144, Checklist for Minutes.
c. On an ongoing basis, coordinators will monitor studies to ensure that continuation review is completed with the time interval of existing approval
d. On an ongoing basis, coordinators will maintain documentation for respective IRBs compiling status of compliance education and other required documentation.
e. Assist in compiling data for IRB Timeline Report

D. ETSU and ETSU/VA IRB Committee

IRB responsibilities include:

a. Reviewing and voting on IRB Policies and Procedures, ensuring that Policies are in compliance with all applicable regulatory requirements, on at least an annual basis
b. Completing a Performance Self-Evaluation (Form 114) on an annual basis each December. Members forward the completed Form 114 to IRB staff.

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E. VA R&D Committee

Responsibilities include:

a. Annually review the ETSU/VA IRB membership and composition, forwarding findings and any recommended adjustments to the ETSU/VA IRB Chair, Director, and the VPR.

F. ETSU Office of Internal Audit

The responsibilities include:

a. Annually review ETSU IRB and ETSU/VA IRB membership and composition for compliance with applicable policies and regulations
b. Audit the Office for the Protection of Human Research Subjects (OPHRS) 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 Tennessee Board of Regents (TBR) policies in addition to government laws and regulations.

The audit report will be forwarded as follows:
Tennessee Board of Regents (TBR), 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, Veterans Health Administration Office of Research Oversight, VISN 9

G. Legal

The ETSU Counsel (Ex-officio IRB member) will consistently provide the IRB and HRPP Administration with legal opinion on the requirements and application of state, local and federal laws relating to the protection of human participants in research. The VA general counsel will also be consulted if necessary. Either counsel make seek further opinions, if necessary, from other lists or offices of jurisprudence, such as the Office of the U.S. Attorney General.

H. External Entities

The OPHRS is additionally audited by external entities, which may include but are not limited to, the FDA, OHRP, ORO, and Association for the Accreditation of Human

Research Protection Programs, Inc. (AHRPP). When these audits occur, a copy of the audit outcome, along with associated responses, will be forwarded to the ETSU Office of Internal Audit.

III. Audits and Compliance Reviews

Audits and compliance reviews are conducted by the ETSU and ETSU IRB in the form of for cause audits and compliance reviews.

Activities may include, but are not limited to the following:

1. interviews of PI, Co-PI and/or research staff
2. review of randomly selected participant files to:
    - determine whether the approved inclusion/exclusion criteria were met
    - Determine that participants were not enrolled until after all appropriate approvals were obtained
    - determine whether the correct informed consent document(s) was utilized and that informed consent was obtained in the manner approved by the IRB
    - Determine whether the approved dose ranges of the study drug were administered
    - Review procedures to determine if consistent with protocol
    - Compare list of subjects (# enrolled/accrued) provided by the Investigator with continuation review report (Form 107) for consistency
3. review of study files to:
    - Determine whether all of the amendments were reported before change implemented unless necessary to eliminate apparent immediate hazard
    - Determine whether UPIRTSOs were reported in a timely manner
4. review of IRB files to:
    - Determine whether ICD complies with federal regulations
    - Determine whether IRB (HRPP) and VA R&D administrative file(s) contain all amendments and adverse reactions submitted by the investigator
    - Determine whether IRB review was timely
    - Determine whether continuation review was completed within one year (or more often if appropriate)
    - Compare grant submissions and progress reports/research descriptions and continuation review reports in the IRB administrative and, if applicable, the ORSPA records files (for funded research) for consistency
    - Confirm completion of compliance education for PI and research personnel
5. observation of the consent process as determined necessary by the convened IRB (i.e, considered when a complaint is received regarding the informed consent process, or when investigator veracity is doubted)

A. For cause audits

For cause audits, which are conducted in response to an identified concern, are conducted to assess compliance with federal regulations, applicable laws and ETSU IRB Policies and Procedures.

Indicators of the need for cause audits may include:

- ETSU or ETSU/VA IRB full committee request
- Response to a complaint, whether internal (participant, etc) or external (sponsor, etc) of potential non-compliance or violations

B. Compliance Reviews

The objectives of compliance reviews are as follows:

1. Determine if investigators implement protocols as approved
2. Determine if written records comply with institutional, industrial, federal, state, local, and VA regulatory requirements
3. Identify issues to be addressed in IRB educational/training initiatives
4. Examine/reevaluate the informed consent process to determine areas in need of improvement
5. Monitor/evaluate responsiveness and reporting regarding participant questions, concerns, withdrawals and complaints
6. Identify areas for (IRB) service improvement

Compliance reviews take place on a variety of studies, selected at random by an IRB Chair for program participation. An initial invitation to participate is extended, by telephone, to the principal investigator (PI) (or designee), and if accepted, will be followed by written confirmation of the audit date, time and site. Upon arrival, the compliance reviewers will deliver a letter of authorization that has been signed by the Chair, Vice Provost for Research and, for research conducted by VA employees or using VA facilities, the Associate Chief of Staff for Research.

At least three compliance reviews per year (to include one VA file per year and one MSHA study per year) will be undertaken. Additional compliance reviews may be conducted if findings warrant additional frequency.

C. Procedures for compliance and for cause audits

Audits and compliance reviews will be conducted by one or more representatives from the Office for the Protection of Human Research Subjects, and if a VA study, one VA R&D administrative member and if possible, an ETSU or ETSU/VA IRB member. For audits conducted for specialized research, requiring particular expertise, an additional

IRB member or other qualified external consultant, may additionally be invited to assist in the review.

Prior to the compliance review or audit, the study file for the particular study is reviewed by the Director, HRPP. Information regarding the number of subjects entered into the study during the last year (as reported on IRB Form 107) is noted along with any UPIRTSO reports, amendments and/or modifications to the protocol. A copy of the most recent informed consent approved will be attached to the IRB Inspection Form. Also included with the IRB Inspection Form, and used as an addendum, is a Supplemental Form for Audits which lists the total number of records or charts reviewed, the subject code/initials/patient ID#, date of signature and any specific comments regarding the consent forms that are actually reviewed at the research site. Information given in the last progress report should correlate with the information in the study file(s). When conducting the on-site review, the person obtaining informed consent may be interviewed to determine how the informed consent was obtained. This information is essential in determining if the informed consent form was adequately reviewed with the subject, concerns were addressed and questions answered. Finally, an exit interview will be conducted with the investigator and any associated research personnel to identify program strengths, areas of deficiency, possible issues to enhance education, and ways in which the IRB can improve services. A written report, proactive and educational in nature, will be developed. If any discrepancies were identified during the records review or interview(s), the report will include recommendations on how deficiencies can be corrected, along with citations of federal regulations and institutional policies, if appropriate.

If subjects are accrued additionally at the VA Medical Center or at any of the Mountain States Health Alliance sites, the hospital files may be cross-referenced. The consent will be reviewed for accuracy, dates, and signatures of all authorized persons. Any discrepancies found will be listed on the IRB Inspection Form. If discrepancies are identified during the audit, additional study records may be conducted. Review of records may include case report forms used in FDA regulated research, original data, and/or pertinent portions of the medical records.

For both compliance reviews and directed audits, the HRPP Director and the IRB Chair will prepare a summary report for presentation to the appropriate convened IRB. Any additional actions required by the IRB will be documented in the minutes. A copy of the summary report, including any additional actions required by the IRB will be copied to the PI, becoming a permanent part of the research record.

If there is an objection to some portion of the compliance review or audit, an investigator may submit an appeal in writing. (Refer to policy: Appeal Process*)*.

IV. External Site Audits

The IRB must be notified of all impending audits.

A copy of all FDA, NIH, NCI (for cooperative group research, such as ECOG, SWOG, etc.), departmental or sponsor announcements of audit and/or letters of warning must be

forwarded to the Director, HRPP and, if applicable, the VA AO, within two (2) working days of receipt. Failure to comply with this policy may result in suspension of human subject approval for a project.

A copy of all responses to audits and/or to letters of warning must be sent to the Director, HRPP, and, if applicable, the VA AO.

V. VA Audits

The VA Research & Development office monitors VA patient records for the following:

The electronic record will be audited to ensure the subject has been identified (under Clinical Warnings) as being enrolled in a research protocol (if flagging was determined to be required by the IRB). The PIs name, study title and point of contact (POC) will also be annotated. The electronic record will also be audited to ensure that a copy of the Informed Consent has been scanned into the medical records.

The ETSU/VA IRB accepts RCO audits to fulfill auditing requirements.

The VA Research Compliance Officer (RCO) forwards the results of all RCO informed consent audits, regardless of outcome, to the IRB in a timely fashion.

The VA RCO also forwards all RCO regulatory audits, regardless of outcome, to the IRB in a timely fashion.

If there is apparent serious or continuing non-compliance, the VA RCO forwards reports within 5 business days; otherwise audit results are forwarded to the IRB at the time of continuing review.

The IRB may require more frequent audits by the research compliance officer or by other means. The IRB also may require the research compliance officer to conduct more focused audits of one or more aspects of the study. The requirement to increase the frequency of audits or to audit specific aspects of the study might be based on considerations including, but not limited to:

- Involvement of vulnerable populations.
- Level of risk
- Phase I or phase II studies
- Involvement of FDA approved drugs for which there has been a new safety warning issued, or change in the labeling that indicates increased risks.
- Issues of non-compliance
- Data confidentiality or security concerns

VI. IRB Review

After reviewing the audit, the IRB may require:

- no action;
- modification of the research protocol;
- modification of the information disclosed during the consent process;
- additional information be provided to past participants;
- notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research);
- requirement that current participants re-consent to participation;
- modification of the continuing review schedule;
- monitoring of the research;
- monitoring of the consent;
- suspension of the research;
- termination of the research;
- obtaining more information pending a final decision
- referral to other organizational entities (e.g., legal counsel, institutional official);

The IRB may require a subsequent audit to evaluate the results of corrective action plans.

References:

VHA Handbook 1058.01, May 21, 2010