

**UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER
INSTITUTIONAL REVIEW BOARD
AUDITING OF RESEARCH STUDIES**

I. PURPOSE

To document the policy and procedures used by the University of Tennessee Health Science Center Institutional Review Board regarding the auditing of IRB-approved studies.

II. SCOPE

This SOP applies to the IRB administrative staff, IRB members, IRB compliance auditing staff, and investigators.

Personnel Responsible:

UTHSC IRB administrative staff, compliance auditing staff.

III. BACKGROUND

Under federal regulations for the protection of human subjects, IRBs must maintain written procedures for ensuring prompt reporting of any unanticipated problems involving risks to subjects or others, or any serious and continuing noncompliance with federal regulations or local IRB policies and procedures. In addition, the regulations require IRBs to conduct continuing review of previously approved research, and specifically authorize IRBs to observe or have a third party observe the consent process and the research as part of the continuing review process.

One component of the IRB's compliance oversight activities involves auditing of previously approved studies. The process of compliance auditing is meant to accomplish several important purposes. First, it is intended to assure that human subjects are properly protected, and that the procedures used to accomplish this goal are carefully documented. Second, the auditing process is intended to assist investigators in complying with the current regulatory standards for protecting human subjects and in avoiding any external sanctions that may result from non-compliance with the standard of practice. Finally, this process is intended to assure that the University and affiliated institutions remain in good standing with federal agencies having oversight of human subjects research activities.

The purpose of this policy is to provide written guidance on operational requirements for compliance auditing activities.

In Accordance With:

For studies approved under the revised Common Rule:

45 CFR 46.108(a)(4); 45 CFR 46.109(a); 45 CFR 46.109(e); 45 CFR 46.111(a)(6); 45 CFR 46.113; and

For studies approved under the Pre-2018 Common Rule:

[45 CFR 46.103\(b\)\(5\)](#); and

For FDA-regulated studies:

21 CFR 56.108(b); 21 CFR 56.109(f); 21 CFR 56.111(a)(6)

Institutional Review Boards Frequently Asked Questions – Information Sheet

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm>

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IV. PROCEDURES

1. The UTHSC IRB will have the authority or may designate a third party to observe the conduct of any research activity, and may review at any time all research records, including but not limited to informed consent documents, regulatory files, IRB files, subjects' research and medical records, clinical materials, storage and distribution of investigational devices (e.g., drugs, devices, or biologics), record storage, computer files, and results of procedures and tests performed during the course of the research.
2. Research compliance auditing staff will also have the authority to observe the informed consent process and to interview subjects either during or after their participation in research activities.

Categories of Audits

3. Primarily there are five types of audits that may be conducted by the UTHSC IRB:
 - a. **Random/Routine:** The IRB Compliance Advisor will randomly select previously approved research studies.
 - b. **Informed Consent:** This audit is intended to support researchers in conducting the informed consent process. It may include observation of

- the consent interview and/or a thorough review of the training of key study personnel obtaining informed consent, review of signatures on informed consent documents, and storage of the informed consent documents.
- c. **For-cause:** This review is performed when concerns regarding compliance, protocol adherence, or subject safety are brought to the attention of the IRB. These audits are performed at the direction of the Director, Associate Director, or the full Board.
 - d. **Training:** This audit is intended to support new researchers, or researchers who initiate projects with no sponsor (private industry or federal) support. The training audit is generally performed shortly after the project receives initial IRB approval.
 - e. **Investigator-Initiated:** An investigator or research coordinator may request an on-site review to assist in keeping records and procedures in compliance with federal regulations and institutional policies or to prepare for an external audit by a sponsor or federal agency.
4. Criteria for choosing studies for audit include, but are not limited to, the following:
- a. Random selection;
 - b. Sufficient cause as determined by the IRB;
 - c. Investigator-initiated projects;
 - d. High risk studies as designated by the Board;
 - e. Any report of suspected noncompliance;
 - f. Research terminated by the IRB due to failure of the investigator to submit the study for continuing review or failure to respond to a request for information from the IRB;
 - g. Verification of continuing review reports; and
 - h. Studies reporting a large number of unanticipated problems, including adverse events and/or protocol deviations.

Audit Notice

5. Prior to initiation of an audit, the investigator will be notified by the IRB Compliance Advisor or designee via project correspondence in iMedRIS and/or email regarding the following types of audits:
 - a. **Random/Routine:** Investigators are contacted to arrange an acceptable date and time for the audit.
 - b. **Informed Consent:** Investigators are contacted to arrange an acceptable date and time for the audit.
 - c. **For-cause:** Investigators are contacted to arrange an acceptable date and time within a few days after the need for the audit has been established.
 - d. **Training:** Investigators are contacted to arrange an acceptable date and time for the audit shortly after the project receives initial IRB approval.

- e. **Investigator-Initiated:** A time will be arranged that is mutually convenient.

The correspondence will instruct the Principal Investigator to submit a completed Pre-Audit form via iMedRIS within two weeks of the request for an audit, unless the audit is for-cause and the request will be to submit the form within one week.

Failure to submit a completed Pre-Audit form within the requested amount of time will result in a second correspondence request copied to the Chair of the department and/or to Research Administration at the hospital/institution.

Elements of Audit Review

- 6. Before the audit, the IRB Compliance Advisor will review the IRB study file and all documentation related to the study including but not limited to:
 - a. Pre-Audit form sent to the IRB via iMedRIS;
 - b. IRB (Form 1) Application;
 - c. Grant application (if applicable);
 - d. Sponsor Protocol (if applicable);
 - e. Investigator's Brochure(s) and/or package inserts;
 - f. Consent form(s);
 - g. Continuation application(s);
 - h. Amendment/Revision request(s);
 - i. DMSB/Annual report(s);
 - j. Advertising/Recruitment materials;
 - k. Adverse events and unanticipated problems;
 - l. Protocol deviation(s);
 - m. iMedRIS correspondence;
 - n. Documents submitted for IRB review;
 - o. IRB minutes; and
 - p. Subsequent publications resulting from IRB-approved protocols may also be reviewed (if appropriate).

- 7. A pre-audit interview may be conducted with the investigator or other key research personnel to document the delegation of authority related to the following activities:
 - a. Regulatory affairs/IRB submissions;
 - b. Obtaining of informed consent;
 - c. Recruitment of study participants;
 - d. Reporting of adverse events/protocol deviations;
 - e. Reporting of injury or other unforeseen events to the IRB/sponsor;

- f. Maintaining study documentation/CRFs;
 - g. Test article accountability;
 - h. Monitoring by the sponsor/CRO; and
 - i. Verification of continuing review reports.
8. During the audit, the investigator or designee will:
- a. Provide the IRB Compliance Advisor with the study files;
 - b. Make available the use of a quiet space for the IRB Compliance Advisor to review the study files;
 - c. Provide a list of all study participants to the auditor;
 - If the number of subjects enrolled is large, the auditor will select a percentage of the subject population to be audited. Otherwise, all records will be reviewed;
 - In the case of a for-cause audit, the IRB may request a 100% audit of study participants' records; and
 - d. The Investigator or designee who is familiar with the study will be available during the audit to address questions of the IRB Compliance Advisor.
9. The UTHSC IRB audit form will be used and may be amended by the auditor to capture all required information necessary for the audit. This audit form will be uploaded to the Audit submission in iMedRIS.
10. Audit reviews may include:
- a. Comprehensive review of IRB records, investigator study records (paper and electronic), and patient medical/dental records;
 - b. Individual subject records to determine whether:
 - Subjects met the inclusion/exclusion criteria;
 - Study-related procedures are performed according to the IRB application and/or protocol;
 - Study-related procedures are scheduled and performed per the study timeline;
 - Data are recorded and stored securely as described in the IRB application and consent form(s);
 - Adverse events have been reported according to institutional policy;
 - Protocol deviations have been reported according to institutional policy;
 - Payments were made to subjects as described in the IRB application and consent form(s); and
 - Subject ID numbers are assigned according to protocol and/or IRB application.

- c. Monitoring of ongoing research to ensure adherence of study procedures as described in the most recently approved version of the IRB application, study protocol, and informed consent;
 - d. Interviews with investigators, staff, and/or subjects;
 - e. Review of specimens and associated documentation and collection processes;
 - f. Review of study medication or device; and
 - g. Review of computer hardware and/or software associated with the research.
11. IRB Compliance Advisor may survey key study personnel to determine the training needs of the research team.

Report of Findings and Follow-up

12. After the Audit, a report of audit findings will be prepared and submitted to the IRB Director or Associate Director for review and action. The report will provide a summary of the findings, including the identification of areas which need improvement and recommendations for improvement. The Director may consult with the full Board regarding corrective action plans necessary to correct deficiencies identified at audit. A copy of the audit report and a letter indicating necessary corrective actions will be sent to the principal investigator, study contact(s), and research administrative specialist (if appropriate) via iMedRIS, the UTHSC IRB electronic system.
13. If the results of the audit identify outstanding issues, a letter outlining the basis for the findings and requesting needed explanations, corrective action plans, and/or study revisions will be sent to the investigator. Note that the corrective action plan may include a request to not include the data and specimens in the final research analysis if the manner in which they were obtained, including the consent process, was not found to be in compliance with federal regulations and institutional policies.
14. If preliminary findings so indicate, the IRB may suspend the study enrollment or activities, or terminate the study and take appropriate action to ensure the safety and welfare of the subjects.
15. The PI may be required to appear before the full Board or to meet with an IRB-appointed investigative subcommittee to address issues identified at audit. However, the PI may not have attorneys or other witnesses present at the meetings.

16. The IRB may engage any outside consultant or expert as necessary to conduct the audit.
17. If subjects are considered at risk due to the actions of the PI or other key research personnel, appropriate officials of the institution in which the research is occurring and the sponsor of the research will be notified, and appropriate action will be taken to ensure the safety and welfare of the subjects.
18. Audit reports, corrective action plans, and correspondence with investigators will be transmitted to appropriate officials of the institution in which the research is occurring as necessary to assure proper protection for the rights and welfare of human subjects.
19. Copies of audit reports and correspondence will be filed in the appropriate electronic study files, as well as in the IRB Compliance Advisor's electronic files. In addition, copies can be located in the Audit submission, which will be placed on the electronic meeting agenda and sent electronically to Board members before the Board meeting each applicable week when the agenda is finalized.
20. Follow-up audits will be scheduled when substantial deficiencies have been identified where correction is crucial in providing adequate protection for the rights and welfare of subjects.