Research Audits PGR

Effective: 10/16/2015
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Name of Associated Policy: Palmetto Health Administrative Research Review

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DEFINITIONS:

1. **Audit**: A systematic and independent examination and verification of trial-related activities, documents, and processes to determine compliance with applicable standards; the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and/or regulatory requirement(s).

2. **Continuing Non-compliance**: A pattern of repeated actions or omissions taken by an Investigator that indicates a deficiency in the ability or willingness of an Investigator to comply with Federal regulations, Palmetto Health policies and/or PGRs, determinations of the Institutional Review Board, or provisions of the approved research study.

3. **Corrective and Preventative Action (CAPA)**: Corrective Action is action taken to eliminate the causes of an existing noncompliance issue or other undesirable situation in order to prevent recurrence. Preventive Action is the action taken to eliminate the causes of a potential noncompliance or other undesirable situation in order to prevent occurrence.
4. **Investigator:** An individual having the background and training in scientific and administrative oversight necessary to conduct and manage research activities.

5. **Non-Compliance:** Failure to follow the regulations, or the requirements or determinations of the IRB.

6. **Research Staff:** Individuals who assist in a research project overseen by an Investigator.

7. **Serious Non-Compliance:** An action or omission taken by an Investigator that any other reasonable Investigator would have foreseen as compromising the rights and welfare of a participant. The following events will in most cases be considered Serious Non-compliance: (i) the conduct of any non-exempt research involving human subjects without IRB review and approval; (ii) enrollment of any human subject in a research study involving greater than minimal risk without informed consent; or (iii) implementation of substantive modifications involving possible risks to human subjects or others without IRB review and approval.

**RESPONSIBLE POSITIONS (TITLE):**

- Research Compliance Monitor
- Principal Investigator
- Research Manager
- Study Staff
- Sub-investigator(s)
- Chair of Institutional Review Board
- Director, Research
- Research Educator

**EQUIPMENT NEEDED:**

N/A

**PROCEDURE STEPS, GUIDELINES OR RECOMMENDATIONS**

1. **PURPOSE**
   1.1. This procedure establishes audit activity as a method to assess compliance.
   1.2. This process begins when information is received.
   1.3. This process ends when information has been filed.

2. **GUIDANCE**
   The Palmetto Health Research Compliance Department is responsible for conducting audits of a) any research conducted at Palmetto Health and b) the Palmetto Health Institutional Review Board (IRB).
   1.1 Audits may include a simultaneous review of both the IRB and the Investigator’s study procedures and documents.
   1.2 The Research Compliance Monitor may use the following standards in the audit process: U.S. Food & Drug Administration’s (FDA) Code of Federal Regulations (CFR 21), Department of Health and Human Services Code of Federal Regulations...
Research Audits PGR


1.3 The goal of the Research Audits is to achieve and maintain compliance in the safety, quality, efficiency, and effectiveness of the research activities performed at Palmetto Health.

1.4 Objectives of the program are to:

1.4.1 Improve compliance of investigator site responsibilities by

1.4.1.1 Helping to establish research focused quality systems that control research activities
1.4.1.2 Sustaining appropriate supervisory oversight
1.4.1.3 Adhering to local and global requirements
1.4.1.4 Controlling investigational products
1.4.1.5 Assuring proper informed consent

1.4.2 Improve compliance of the IRB responsibilities by

1.4.2.1 Helping to establish quality systems
1.4.2.2 Adhering to local and global requirements

1.5 The measures of the quality improvement program are defined in:

1.5.1 Research Audit Tool

1.6 The number of audits to be completed by the Research Compliance Monitor will be at least six during the course of one year, barring any unforeseen circumstances and/or unanticipated lengthy audit cases.

3. PROCEDURE / AUDIT TYPES

3.1. For Cause Audits: The For Cause Audit is performed when a question of non-compliance, research integrity or misconduct exists.

3.1.1. Allegations of noncompliance resulting in a for cause audit may be received by Research Compliance from a variety of internal and external sources which may include, but is not limited to:

- the Chair and members of the IRB
- investigators and other research personnel
- sponsors of research
- institutional officials
- Palmetto Health Corporate Compliance
- Palmetto Health Audit Services
- Palmetto Health Regulatory Compliance
- employees of Palmetto Health
- members of the medical staffs of our hospitals and clinics
- research subjects and their families
- citizens in the community

3.1.2. All allegations meeting the definition of major (allegations of non-compliance with a high risk of human subject violations) will immediately prompt a full audit.

3.1.3. In the event that scientific misconduct is alleged, the Palmetto Health Research Misconduct Policy will be followed.

3.1.4. For-cause audits and for-cause targeted reviews receive priority status over those which are randomly selected.
3.2. **Targeted Reviews**: Targeted reviews use auditing techniques, yet due to their specific nature, are abbreviated auditing assessments used to:
- Assess the need for a full audit
- Confirm compliance in specific areas of a given research study
- Gather data in order to render an opinion on specific study practices

3.2.1. Allegations of noncompliance resulting in a targeted review may be received by Research Compliance from the sources listed in 3.1.1.

3.2.2. Targeted reviews examine a sufficient sample of study files to gain an assessment of the nature of any research problems.
- The sample selected contains files known to be involved in the issue at hand along with files that are not thought to have research integrity issues.
- The sample size and selection method along with the audit methodology will be at the discretion of the Research Compliance Monitor.

3.2.3. Significant findings from a targeted review would be those that 1) indicate serious non-compliance, 2) violate federal requirements or policies and/or 3) cumulative violations of the same nature. A significant finding may indicate a need for a full audit.

3.2.4. Research Compliance and the Institutional Review Board may refer a new investigator to undergo a targeted review. The targeted areas of review may focus on informed consents, essential documents, source verification, financial documentation, contracts, and/or research processes.

3.3. **Random Audits**: All active Palmetto Health IRB-approved clinical research projects have an equal chance of being selected to undergo an audit.

3.3.1. A list of the active Palmetto Health IRB-approved clinical research projects is obtained by the Research Compliance Monitor.

3.3.2. The list is divided into two separate lists: one list for FDA regulated studies, and one for non-FDA regulated studies (investigator initiated, sponsor-initiated device studies, etc.)

3.3.3. Using a random number generator, one study from each list is randomly selected to undergo an audit. Generally, a targeted review is performed on randomly selected audits but may require a full audit depending on the findings of the targeted review.

3.3.4. Research studies that have been randomly audited by Palmetto Health in the past 3 years will not be considered for another randomized audit; however, this does not exclude them from for-cause audits/targeted reviews or follow-up audits.

3.3.5. In a random audit, a minimum of 10% of the subjects enrolled will be initially chosen to be reviewed.
- This 10% should include those subjects with PH IRB reports of death and serious and unexpected adverse events, if applicable.
- A minimum of three subject’s documents will be reviewed.

4. **PREPARATION FOR THE AUDIT**

4.1. Selection of audit is done on a priority basis. Any type of for-cause audits are first priority.

4.2. Assign a file number to the audit (#year – sequential number)
4.3. Notification to the Principal Investigator (PI)/Research Manager of intent to audit.
4.4. Contact is made to the PI/Research Manager’s office to discuss the study audit selection and schedule of the audit.
4.5. A formal notification letter is mailed and emailed, if applicable, to the PI/Research Manager addressing details of the audit and a copy of this PGR is provided.
4.6. Arrange a mutually convenient time as soon as possible from the initial audit notification.
4.7. If applicable, confirm the audit details in writing indicating the time, date, and place of audit.
4.8. Determine which processes and industry standards for study conduct are in place prior to the audit.
4.9. Where the standards are not specifically listed, determine which standards apply
4.10. Prior to the initiation of an investigator audit, applicable documents may be reviewed. These documents may include, but are not limited to the following:
   - Regulatory documents: copies of all IRB approvals and disapprovals
   - Approved protocol and all amendments with signature pages
   - Informed consents and associated versions
   - Current Investigator’s Brochure or Instructions for Use

5. PERFORMANCE OF THE AUDIT
5.1. **IRB Review**
   5.1.1. Perform oversight review of IRB activities (if applicable to include, but not limited to):
      - Ensure proper use of expedited, exempt, full-board review types
      - Proper documentation of waivers and alterations
      - Proper continuation reviews in accordance with initial approval time table
      - Completeness of project/study files
      - Adequacy of resources to support IRB operations
      - Documented procedures for operation of IRB and for research involving human subjects

5.2. **Investigator Site**
   5.2.1. A meeting is conducted with the Investigator, Research Staff and any other relevant study personnel to provide an overview of the audit process and introduce audit staff. Key study staff is interviewed to gain an understanding of the research processes used for protocol management.
   5.2.2. A tour is taken of all local facilities used in research conduct.
   5.2.3. Review of specific study documents to independently verify study data. Source documents may include, but are not limited to the following:
      - Inpatient and outpatient patient records (progress notes, diagnostic reports, laboratory data, admission forms)
      - Essential regulatory documents
      - Informed Consents
      - Drug or Device Accountability Logs
      - Protocol required procedures and assessments
      - Enrollment tracking logs
      - Pharmacy records
      - Financial records
      - Other pertinent study documents and records
5.2.4. Subject records may be reviewed for deficiencies in the following categories:

- Properly signed and dated informed consent
- Eligibility
- Correct treatment and treatment sequence
- Evaluation of disease/outcome/response
- Adverse events and/or Serious Adverse Events related or unrelated to treatment
- Investigational or product accountability
- Investigator oversight
- Personnel delegation
- Overall training and experience

5.2.5. Assess study data quality, reliability, and integrity to determine overall compliance.

5.2.6. Determine whether the standards identified during the preliminary review are being adhered to properly.

5.2.7. When subject safety issues are observed during an audit, the Research Compliance Monitor notifies the Director of Research to determine appropriate actions, if any, to secure compliance.

5.2.8. Certain situations related to research audits may require protection under the attorney-client privilege.

6. REPORTING

6.1. Investigator Site

6.1.1. Research Compliance Monitor schedules an exit meeting with Investigator and relevant Research Staff

- Findings and any immediate corrections made by staff are reviewed
- Recommendations for corrective action(s) may be discussed
- An audit certificate is given to the PI for their study files indicating the date(s) of the audit and names of auditing team members

6.1.2. An Interim Report is prepared to include general audit finding trends and/or noncompliance.

6.1.2.1. The Interim Report is reviewed by the Palmetto Health IRB Administration Manager to determine if any of the audit findings meet the definition of serious non-compliance and/or continuing non-compliance.

6.1.2.1.1. Any audit report with a finding that meets the definition of serious non-compliance and/or continuing non-compliance will be presented to the PH IRB at the next scheduled IRB meeting.

6.1.2.1.1.1. Any comments, recommendations and/or directives from the IRB regarding serious non-compliance and/or continuing non-compliance will be sent to the Principal Investigator from the PH IRB.

6.1.2.1.2. Regulatory agencies will be notified per federal guidelines.

6.1.2.1.3. A statement requiring compliance with PH IRB and other regulatory agencies’
directives will be included in the recommendation section of the interim audit report.

6.1.2.1.2. Any audit report that does not have a finding that meets the definition of serious non-compliance and/or continuing non-compliance will be sent directly to the Principal Investigator, Research Director, Clinic Manager or Clinical Trials Manager, if applicable.

6.1.2.2. The Interim Report may be reviewed by other Palmetto Health Departments (i.e. Corporate Counsel, Corporate Compliance, and Audit Services) for recommendations as needed.

6.1.3. Investigator Response and Plan of Action: The investigator is given a predetermined timeframe appropriate to the findings to respond to the Interim Report

- Response to findings may be outlined and detailed in a response to the audit report or a corrective and preventative action (CAPA) plan, if indicated.
- The goal of the site’s audit response or CAPA plan will be to establish and maintain compliance.

6.1.4. Palmetto Health Regulatory Compliance may be contacted if any regulatory compliance issues arise or are noted during the audit.

6.2. IRB

6.2.1. A meeting with the IRB Administration Manager and/or Chair of the IRB may be arranged to review audit findings, if necessary.

6.2.2. An Interim Report is prepared to include general audit finding trends and/or noncompliance.

6.2.2.1. The Interim Report is reviewed by the Palmetto Health IRB Manager to determine if any of the audit findings meet the definition of serious non-compliance and/or continuing non-compliance.

6.2.2.1.1. Any audit report with a finding that meets the definition of serious non-compliance and/or continuing non-compliance will be presented to the PH IRB at the next scheduled IRB meeting.

6.2.2.1.1.1. Any comments, recommendations and/or directives from the IRB regarding serious non-compliance and/or continuing non-compliance will be sent to the IRB Chairman and the IRB Manager.

6.2.2.1.2. Regulatory agencies will be notified per federal guidelines.

6.2.2.1.3. A statement requiring compliance with PH IRB and other regulatory agencies’ directives will be included in the recommendation section of the interim audit report.

6.2.2.1.2. Any audit report that does not have a finding that meets the definition of serious non-compliance and/or continuing non-compliance will be sent directly to the Research Director, IRB Chairman and the IRB Manager.
6.2.2.2. The Interim Report may be reviewed by other Palmetto Health Departments (i.e. Corporate Counsel, Corporate Compliance, and Audit Services) for recommendations as needed.

6.2.3. IRB Administration Manager Response and Plan of Action: The manager is given a timeframe appropriate to the findings to respond in a timely fashion to the Interim Report

6.2.3.1. Response to findings may be outlined and detailed in a response to the audit report or a corrective and preventative action (CAPA) plan, if indicated.

6.2.3.2. The goal of the IRB’s audit response or CAPA plan will be to establish and maintain compliance.

6.3. Audit reports are considered confidential internal documents and shall be distributed by the Palmetto Health Research Compliance Department.

6.3.1. All audit reports will contain a legal statement that includes the following:

6.3.1.1. Audit reports are not to be released to external regulatory agencies or others without the written consent of the Palmetto Health Research Division.

6.3.1.2. Audit reports shall not be shared with sponsoring organizations, contract research organizations or individuals acting on the behalf of a research sponsor.

7. CLOSURE

7.1. Final audit reports will incorporate both the Principal Investigator’s and Research Manager’s audit response.

7.2. The final audit report is submitted to the Research Director and the Chair of IRB for response and any additional actions indicated either by Research Compliance, the IRB, or others, as necessary.

7.3. Interim or final audit reports may be presented to the IRB by the Research Compliance Monitor for comment and/or directives.

7.4. If issues of non-compliance, serious and/or continuing, were determined by the IRB, the Research Compliance Monitor will file a physician occurrence report and assist PH Medical Staff Affairs as necessary.

8. EDUCATION

8.1. The Research Compliance Monitor may be a resource for assisting in writing audit responses as well as writing and implementing CAPA Plans.

8.2. The Research Educator and Research Compliance Monitor may use audit findings to collaborate and provide any identified education to sites, investigators, and research staff as well as other supportive actions, as warranted.

9. FOLLOW UP

9.1. Follow up audits may be performed as indicated by the Research Compliance Monitor, IRB, and/or Director of Research, or others.

9.2. The Research Compliance Monitor will follow up with the responsible personnel on a periodic basis and near the follow up action completion dates committed by management.

9.3. Upon obtaining sufficient evidence that follow up action has been implemented, the Research Compliance Monitor will note the status of the action with an addendum on the
final report.

9.4. Past due findings, where necessary actions have not been taken by implementation dates, are reported to the Director of Research, Institutional Review Board, and/or Palmetto Health’s Designated Institutional Official for Research and/or the Vice President over the area with the past due findings.

10. REPORT RETENTION

10.1. The final audit report is an internal document, filed in a locked cabinet in the Research Compliance Department.

10.2. Any report that contains confidential information will be securely preserved and monitored to prevent unauthorized access, removal, or disclosure.

10.3. Records that have satisfied their required retention period of ten years will be destroyed.

REFERENCES

International Conference on Harmonisation (ICH) 1.6

Policies and PGRs of the Palmetto Health Institutional Review Board

Research Misconduct