The Ohio State University

College of Medicine Office of Research

Clinical Research Compliance Assessment Manual

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Version 6
Procedural

Prepared by the College of Medicine Office of Research Compliance Program
INTRODUCTION
The primary objective of The Ohio State University College of Medicine Office of Research (COMOR) Clinical Research Compliance Assessment program is to ensure the appropriate management and oversight of clinical research within the College of Medicine. Multiple regulations apply to the conduct of clinical research. Failure to meet these regulations and requirements may result in research subject harm, invalidation of study results, financial penalties, and reputational harm for OSU. The compliance assessment is an opportunity for research study teams to proactively recognize and address potential issues before developing into violations.

The Principal Investigator (PI) is ultimately responsible for the overall conduct of the research, appropriate delegation of tasks, and compliance with applicable laws and policies. Regardless, it is the responsibility of all members of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the protocol and standard operating procedures (SOPs) and execute tasks as delegated in compliance with regulatory requirements and institutional policies.

ASSESSMENT OBJECTIVES
COMOR may conduct routine and directed (for cause) assessments of any clinical research activity conducted within the College of Medicine. COMOR will select clinical research activities for routine assessments on the basis of a risk analysis based on research subject risk and regulatory complexity. Directed assessments can be requested by the IRB, Office of Responsible Research Practices, institutional officials or as a result of any official complaint.

The clinical research compliance assessment is a systematic and independent examination of study-related activities for the following:

- Oversight and appropriate delegation of tasks
- Screening and consenting process
- Safety of clinical research participants
- Validity and integrity of the data
- Compliance with the approved research protocol
- Investigational product management and accountability
- Compliance with regulatory requirements
- Compliance with institutional standards and policies

The exact items reviewed during the compliance assessment will depend on the activity and applicable regulations. Appendix A lists the general elements as well as corresponding documents that may be requested in an assessment.

Content reviewed in routine assessments is directed by risk-based methodology rather than complete source data verification. Therefore, an absence of observations does not imply a guarantee of the absolute integrity of the data that was inspected nor the ability of the research to stand up to an FDA, sponsor, or other institutional audit or review.
COMPLIANCE ASSESSMENT NOTIFICATION PROCEDURES

Scheduling

- The PI will be notified of the compliance assessment by email and provided a copy of the Clinical Research Compliance Assessment Manual. COMOR staff will provide the PI and research support staff with 3 available dates for the Opening Meeting. The PI and research support staff will have **10 business days** to schedule an agreed upon date.
- A copy of the most currently IRB approved protocol, consent forms, and HIPAA authorization forms will be sent by the research team to COMOR staff at the time of scheduling the Opening Meeting.

Active Review

- The compliance assessment will begin with an Opening Meeting. Attendees will include the PI, COM Regulatory Manager(s), lead study coordinator, and additional key personnel. The PI is not required to attend if he or she has had a trial reviewed by COMOR in the last 2 years with an Acceptable outcome.
- During the Opening Meeting, the PI and research team will be asked to provide a short narrative of the protocol, for instance how subjects are recruited and consented, how drug/device is accounted and dispensed, research documentation in the chart, and any protocol deviation or safety reporting. This meeting also allows COMOR staff to further elaborate on the Compliance Assessment process and answer any questions or concerns.
- During the active protocol review period, all source documents for the study must be made available for review. If documentation exists only in electronic format, an electronic copy of these materials should be transferred to a jump drive for COMOR staff to use for review. Members of the research team should be made available to answer questions that may arise during the compliance assessment process.
- A random sample of subjects will be selected for the assessment; however, all subjects may be reviewed. Actual subjects reviewed will be listed in the Initial Observations.

Reporting and Resolution

- A written summary of the initial observations will be sent to the PI and study team. The PI and study team can request an in-person meeting with COMOR staff to review the initial observations.
- The PI will have **15 business days** from receipt of initial observation report to respond in writing. The response should include details of corrective actions to be implemented, if applicable.
- A Final Compliance Evaluation Report will be sent to the PI after considering the additional information provided in the written response. A summaries of compliance assessments will be reported to the Vice Dean of Research.
- The Final Compliance Evaluation Report may include recommendations for corrective actions of findings, up to and including self-reporting to the Institutional Review Board. The PI is ultimately responsible for determining whether any Compliance Assessment findings need to be reported.
• If the PI and research team fail to respond within the required time period or if there are potential human subject violations, the Final Compliance Evaluation Report will be deemed Unacceptable. Trials deemed unacceptable are subject to suspension or closure at the discretion of the Vice Dean of Research. Others outside of COMOR may be notified of the findings and study status.

COMPLIANCE ASSESSMENT OUTCOMES
One of four assessment outcomes below will be noted in the Final Compliance Evaluation Report.

Acceptable: No Deficiencies/Minor Deficiencies Resolved
No deficiencies identified; compliance with all regulatory and investigational product assessments; minor deficiencies identified but were addressed promptly when identified during the compliance assessment.

Acceptable: Minor Deficiencies, Follow-up Required
Multiple minor deficiencies identified. PI indicates that matters will be addressed and implements a corrective action plan.

Opportunities Exist: Major Deficiency(ies), Follow-up Required
Major deficiency(ies) and/or non-compliant categories identified; excessive number of minor deficiencies identified that indicates systemic problems.

Unacceptable: Immediate Attention Required
Deficiency(ies) discovered that may negatively impact research subject(s) immediate safety, OSU’s reputation, or may be a severe regulatory violation. The Department Chair and COM Administration leadership will be notified immediately and the trial is subject to suspension or closure at the discretion of the Vice Dean of Research. Corrective action plan(s) will be developed with input from Department Chair and COM Administration leadership.
### APPLICABLE REGULATIONS AND POLICIES

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**History**

Issued: 1/21/2011
Revised: 11/18/2011, 2/14/2014, 1/25/2016, 10/12/2016, 6/12/2017
Edited: 4/29/2011
Appendix A

ITEMS TO BE ASSESSED

The following items may be reviewed during the compliance assessment, as they apply to the specific research study being evaluated. *Electronic versions of documents are acceptable, as long as they are made available to the person(s) reviewing the research.*

**Documentation**
- Copies of signed Form FDA 1572 (drug or biologic studies) or Investigator Agreement (device studies)
- Copies of CVs, medical licenses, and study-specific financial disclosures
- Current versions of protocol, informed consent, HIPAA Authorization form, investigator’s brochure/device manual, data collection forms, any patient materials, any other IRB approved materials
- IRB submissions and approvals
- Submissions to the FDA, including but not limited to initial IND/IDE application, annual reports, amendments, safety reports, and any relevant communication
- Submissions and approvals to any other necessary committees or regulatory bodies (e.g. Institutional Biosafety Committee, scientific review boards, radiation safety boards, etc.)
- Delegation of Authority log
- SOP Training log
- Training documentation
- Laboratory credentials for all labs
- Investigational product (IP) accountability
- Screening and Enrollment logs
- Adverse Event documentation
- Protocol Deviation Log, Note to File(s)
- Submission of Data Safety Monitoring Board/Committee report

**Activities**
- *Participant screening and enrollment*
  - Verification study personnel did not access medical records or record protected health information (PHI) without proper approval (written authorization or HIPAA waiver as applicable)
  - Verification of appropriate access of screened subjects by study personnel
  - Sufficient source documentation to verify that participant meets eligibility criteria
  - Documentation of eligibility verification by the PI or other qualified study team member
  - Verification that no protocol specific procedures/interventions occurred prior to participant consent
  - Verification study subjects were enrolled during IRB approval period and within enrollment limit

- *Protocol Adherence*
  - Verification that research activities were executed according to the protocol
• Documentation that the participant was updated/re-consented regarding any significant changes to the research that may affect his/her desire to participate
• Proper documentation of any protocol deviations
• Verification any unblinding was carried out according to protocol

• Adverse events
  o Verification that PI and any relevant study staff are reviewing external safety reports
  o Verification of reportable events to sponsor, IRB, DSMB within appropriate time frame
  o Type, grade, and attribution assessed by PI or qualified study personnel

• Data management
  o Proper submission to and review by the Data Safety Monitoring Board/Committee per the protocol
  o Verification data is obtained, recorded, stored, and disposed of according to the protocol
  o Subject associated to protocol in EMR, and associated research documentation in EMR is appropriate and routed to PI or qualified study personnel (if applicable)

• PI Oversight
  o Training of all study personnel on protocol, study-specific procedures before delegation
  o Appropriate delegating of study-related duties based on education, training, and experience
  o Adequate supervision of the conduct of trial, including timely review of subject eligibility, informed consent, case report forms, laboratory tests, and event reports.