***Monitoring and Audit Visits***

1. **PURPOSE**

This Standard Operating Procedure (SOP) describes the procedures, processes, and responsibilities of research team members who coordinate the clinical trial site monitoring and audit visits. University of Michigan research oversight entities may audit clinical trials at any time over the course of the trial. The nature of the audit may be ‘for cause’ or ‘not for cause’. External entities such as funding agencies, sponsors, and the FDA may also audit clinical trials at any given time. Trial documentation and quality control processes, including monitoring, must be maintained to ensure compliance with the protocol and regulatory authorities is evident in the event of an audit.

(**MANDATORY LANGUAGE**)

1. **SCOPE**

This Standard Operating Procedure applies to all members of the research team involved with monitoring and audit visits. This includes tasks involving the preparation, attendance, documentation, and follow-up for the visit. FDA inspections and visits are out of scope for this SOP.

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*[Optional: Insert any additional details necessary to further define the scope of this SOP.]*

1. **POLICY**

This Standard Operating Procedure supports the Good Clinical Practices (GCP) guidelines established by the International Conference on Harmonization (ICH). Section 5.18.1 clarifies the purposes of trial monitoring, which are to *verify that: a) the rights and well-being of human subjects are protected; b) the reported trial data are accurate, complete and verifiable from source documents; and c) the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).*

Furthermore, ICH Section 5.18.3 states that the determination of the nature and extent of monitoring should be based on considerations such as the purpose of the clinical trial, the size, complexity, and objectives of the trial.

Audits are addressed in ICH Section 5.19, which states *the purpose of a sponsor’s audit, which is independent of and separate from routine monitoring or quality control functions, should be to evaluate trial conduct and compliance with the protocol, SOPs, GCP, and the applicable regulatory requirements.*

FDA Regulation ☐ N/A

*[If this SOP is not intended for FDA regulated clinical trials, check the N/A box]*

Per code 21CFR312.53(d) *A sponsor shall select a monitor qualified by training and experience to monitor the progress of the investigation.*

As it pertains to investigational devices, Code 21CFR812.43(d) states: *A sponsor shall select monitors qualified by training and experience to monitor the investigational study in accordance with this part and other applicable FDA regulations.*

National Institutes of Health (NIH) ☐ N/A

*[If this SOP is not intended for NIH clinical trials, check the N/A box]*

For each NIH-supported clinical trial, NIH requires a data and safety monitoring plan that will provide oversight and monitoring to ensure the safety of participants and the validity and integrity of the data. The level of monitoring should be commensurate with the risks and the size and complexity of the clinical trial. A detailed data and safety monitoring plan must be submitted to the applicant's IRB and subsequently to the awarding Institute/Center for approval prior to the accrual of human subjects.

University of Michigan

According to the University of Michigan Institutional Review Board (IRB)

*The IRB office may monitor studies both “for cause” (e.g. alleged non-compliance) and “not-for-cause” (e.g. random review for quality assurance purposes).*

The U-M Office of Human Research Compliance Review (OHRCR), an office of the U-M Office of Research (UMOR) may also conduct post-IRB approval reviews of a routine nature, “for cause”, or “not-for-cause”.

(**MANDATORY LANGUAGE**)

**Additional Regulations or Policies ☐ N/A**

*[Optional: Insert any additional project, department, sponsor, institution, state or federal policies that apply]*

1. **DEFINITIONS**

AUDIT: A systematic review, inspection, or verification, typically conducted by an independent individual or group. An audit may also include examination of compliance with applicable award terms, laws, regulations and policies

DOCUMENTATION: All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken

FOR-CAUSE AUDIT/REVIEW: An audit of research and/or investigators initiated at the request of the IRB or Institutional Official to obtain or verify information necessary to ensure compliance with regulations and institutional requirements and to inform decisions about the conduct of human subject research and/or human subject protection

MONITOR: Designated individual selected by a sponsor or contract research organization to oversee the progress of a clinical investigation

MONITORING PLAN: A document that describes the study-specific monitoring to be performed

MONITORING REPORT: A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor’s SOPs

OTHER REPORTABLE INFORMATION OR OCCURRENCE (ORIO): Any event, not an adverse event, that occurs during a clinical research study

 (**MANDATORY LANGUAGE**)

*[Optional: Insert any additional definitions for technical or special terms used within the Standard Operating Procedure that may not be familiar to the lay reader]*

**Note:** Many of the definitions above were obtained from the IRBMed Glossary. These definitions were current as of 28-Jul-2015 and are subject to change. Please see the [IRBMed Glossary](http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/glossary) for the most current definitions and additional guidance.

 (**MANDATORY LANGUAGE**)

1. **ROLES AND RESPONSIBILITIES**

**Principal Investigator/Designee**

An individual filling the role of Principal Investigator (PI) is responsible for conducting a clinical trial in compliance with the protocol and regulatory requirements. The PI shall be responsible for the following activities:

* Ensures the clinical trial is monitored by qualified personnel not directly involved in the selection of participants or in the implementation of the research
* Works with the clinical trial monitor to implement a monitoring plan
* Ensures the availability of clinical trial documentation for the monitor and auditor’s review
* Corrects and addresses all questions and concerns identified during the visit with the monitor
* Reports monitoring and audit outcomes to the sponsor
* Ensures copies of correspondence with monitor and sponsor are maintained in study records
* Ensures copies of all written correspondence received and sent to external oversight entities are submitted to the IRB Committee

(**MANDATORY LANGUAGE**)

*[Optional: Insert any additional details regarding the responsibilities of the Principal Investigator/Designee*]

**Study Coordinator(s)/Designee**

An individual filling this role may be responsible for the following activities:

* Reviews the clinical trial protocol and other clinical trial documentation in preparation for monitoring visit
* Ensures all study documentation and regulatory materials are up-to-date and available
* Secures physical space for the monitor or auditor
* Ensures applicable staff are available to the monitor/auditor during the visit
* Coordinates visits to the clinical trial pharmacy and lab, when applicable
* Works with research team members to provide responses to all monitoring/audit queries and monitoring/audit reports
* Provides documentation that all monitoring items have been addressed and responds to all queries
* Submits the final monitoring and/or auditing report to the IRB

(**MANDATORY LANGUAGE**)

*[Optional: Insert any additional details regarding the responsibilities of the Study Coordinator/Designee*]

**Additional Roles and Responsibilities**  **☐ N/A**

**(MANDATORY LANGUAGE)**

*[Optional: Insert any additional role(s) and responsibilities that apply to this SOP]*

1. **PROCEDURE**

**Monitoring /Audit Visit Notification**

*[Describe the process for notifying required institutional officials (IRBMED, Regulatory Affairs, Health System, Legal Office, as applicable) of a pending monitoring visit or audit]*

**Monitoring Visit Preparation**

*[Describe the process for preparing for a monitoring visit including preparation of physical space, clinical trial files, regulatory documents, etc.]*

**Audit Visit Preparation**

*[Describe the process for preparing for an audit, including preparation of physical space, clinical trial files, regulatory documents, etc.]*

**Monitoring /Audit Visit Participation**

*[Describe the process for ensuring adequate information, access to records and appropriate clinical trial personnel are available for the monitor/auditor. Include a plan for coverage of an absent research team member.]*

**Monitoring/Audit Visit Follow-up**

*[Describe the process for preparing responses to monitor queries, and for maintaining and disseminating visit/audit documentation that includes correspondence, monitoring reports, institutional reporting and responses to monitoring/auditing entities.]*

**Additional Procedures** **☐ N/A**

*[Optional: Insert any additional relevant procedures. Provide enough detail to ensure the procedure is consistently carried out, without providing so much detail that violations occur due to normal or expected variations in the work.]*

1. **REFERENCES**

FDA Basics - What does FDA inspect?

<http://www.fda.gov/AboutFDA/Transparency/Basics/ucm194888.htm>

International Conference on Harmonisation

<http://www.ich.org/>

NIH Glossary and Acronym List

<http://grants.nih.gov/grants/glossary.htm>

University of Michigan - Quality Assurance and Research Compliance Operations Manual

<http://www.hrpp.umich.edu/om/Part12.html>

University of Michigan - Medical School Institutional Review Board (IRBMED) Glossary

<http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/glossary>

University of Michigan - Medical School Institutional Review Board (IRBMED) Standard Operating Procedures (SOPs)

<http://medicine.umich.edu/medschool/research/office-research/institutional-review-boards/guidance/standard-operating-procedures>

University of Michigan - Office of Human Research Compliance Review (OHRCR)

<http://research-compliance.umich.edu/office-human-research-compliance-review-ohrcr>

(**MANDATORY LANGUAGE**)

*[Optional: Insert any additional SOP references]*

1. **APPENDICES**

(**MANDATORY LANGUAGE**)

*[Optional: Insert any additional SOP appendices]*