***Monitoring and Audit Visits***

1. **PURPOSE**

This Standard - Practice Guideline (SPG) 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 Practice Guideline (SPG) 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. NIH monitoring requirements, FDA inspections and FDA 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**

**Good Clinical Practice (ICH GCP)**

This Standard Practice Guideline supports the Good Clinical Practices (ICH GCP) guidelines established by the International Council 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(s)** (if applicable) [ ]  **N/A**

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

Per Code 21 CFR 312.53(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 21 CFR 812.43(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.*

**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 Research Compliance Review (ORCR), 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.”

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**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 (ICH-GCP R2 definition)

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 (IRB definition)

INTERNATIONAL COUNCIL ON HARMONISATION (ICH): A joint initiative involving both regulators and research-based industry representatives of the European Union, Japan, and the USA in scientific and technical discussions of the testing procedures required to assess and ensure the safety, quality, and efficacy of medicines

MONITOR: An individual who acts as a liaison between the sponsor and the investigator of a clinical study, and who oversees the progress and conduct of the trial; may also be referred to as a Clinical Research Associate (CRA)

MONITORING PLAN: A document that describes the strategy, methods, responsibilities, and requirements for monitoring the trial

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 (IRB definition)

 (**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:** Some of the definitions above were obtained from the IRBMed Glossary. These definitions were current as of 01-Oct-2022 and are subject to change. Please see the [IRBMed Glossary](https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/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 ultimately *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 (when applicable) by qualified personnel
* Works with the clinical trial monitor to implement a monitoring plan (when applicable)
* Ensures the availability of clinical trial documentation for the monitor and auditor’s review
* Acknowledges and responds to all questions, queries, and concerns identified during the visit with the monitor
* 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
* Delegates responsibilities when appropriate

(**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
* Ensures AEs/SAEs, UaPs, deviations, and any other ORIOs have been documented and reported per protocol
* Ensures data entry into the study database is completed prior to the monitor’s arrival
* Schedules and secures physical space and equipment for the monitor or auditor for onsite monitoring/audit visits
* 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 reports
* Request monitoring access to the Electronic Medical Record (EMR) if necessary
* Provides documentation to verify that all monitoring items have been addressed
* Submits all monitoring and/or auditing reports/summaries 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>

FDA Title 21 CFR 312.53 - Selecting investigators and monitors:

<http://www.ecfr.gov/cgi-bin/text-idx?SID=e37712a7ee32d29b3075c4dbe39a860e&mc=true&node=se21.5.312_153&rgn=div8>

FDA Title 21 CFR 812.43 - Selecting investigators and monitors:

<http://www.ecfr.gov/cgi-bin/text-idx?SID=e37712a7ee32d29b3075c4dbe39a860e&mc=true&node=se21.8.812_143&rgn=div8>

International Council for Harmonisation

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

<https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>

University of Michigan - Quality Assurance and Research Compliance Operations Manual

 <https://research-compliance.umich.edu/sites/default/files/resource-download/hrpp_operationsmanual.pdf#page=132>

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

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

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

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

University of Michigan - Office of Research Compliance Review (ORCR)

<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]*