***Noncompliance in Clinical Trials***

1. **PURPOSE**

This Standard Operating Procedure (SOP) describes the procedures, processes, and responsibilities for communicating, documenting, and reporting clinical research noncompliance and escalating cases of noncompliance for clinical trial.

(**MANDATORY LANGUAGE**)

1. **SCOPE**

This SOP applies to all research staff involved in the conduct and management of clinical trials and their interactions with associated clinical research subjects.

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

1. **POLICY**

This SOP supports the Good Clinical Practices (GCP) guidelines established by the International Conference on Harmonization (ICH). Section 4.5.3 states *The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.*

In addition, Section 5.20.1 stipulates *noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution, or by a member(s) of the sponsor’s staff should lead to prompt action by the sponsor to secure compliance.*

Finally, ICH Section 5.20.2 makes note of actions to be taken for serious and/or persistent noncompliance, indicating *If the monitoring and/or auditing identifies serious and/or persistent noncompliance on the part of an investigator/institution, the sponsor should terminate the investigator’s/institution’s participation in the trial.*

**FDA Regulation**  ☐ N/A

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

21 CFR 56.108(b) requires that the IRB follow shall follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of:

1. Any unanticipated problems involving risks to human subjects or others;
2. Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or
3. Any suspension or termination of IRB approval.

University of Michigan Office of Human Research Participant Protection (HRPP)

*The HRPP promotes an organizational culture that encourages a commitment to compliance with the legal, regulatory, and ethical principles that govern human subjects research. The program relies on a system of self-regulation and integrated oversight to accomplish this objective and reflects an emphasis on the high ethical standards and values demanded of the most outstanding research institutions.*

*Generally, allegations of potential noncompliance related to specific research projects are first reviewed by the responsible IRB. IRBs may take interim actions as noted in their SOPs - including suspension of research - to protect human subjects while a concern is under review.*

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

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

1. **DEFINITIONS**

COMPLIANCE: In relation to research: Adherence to all relevant trial-related requirements, good clinical practice (GCP) requirements, and the applicable institutional, state and federal regulatory requirements.

CONTINUING NONCOMPLIANCE: Non-compliance (serious or non-serious) that has been previously reported, or a pattern of ongoing activities that indicate a lack of understanding of human subjects protection requirements that may affect research participants or the validity of the research and suggest the potential for future noncompliance without intervention. Examples of continuing non-compliance may include but are not limited to: repeated failures to provide or review progress reports resulting in lapses of IRB approval, inadequate oversight of ongoing research, or failure to respond to or resolve previous allegations or findings of noncompliance.

NONCOMPLIANCE: The failure of a person or organization to act in accordance with the requirements of a law, regulation, policy, or the requirements and/or determinations of an IRB.

SERIOUS NONCOMPLIANCE: Noncompliance that materially increases risks or causes substantive harm to research participants or materially compromises the rights or welfare of participants, including consideration of the following:

* Harm to participants;
* Exposure of participants to a significant risk of substantive harm;
* Compromised privacy and confidentiality of participants;
* Willful or knowing misconduct on the part of the investigator;
* A violation of ethical principles; or
* Damage caused to the scientific integrity of the data collected.

OFFICE OF HUMAN RESEARCH COMPLIANCE REVIEW (OHRCR): A component of the University's [Human Research Protections Program (HRPP)](http://research-compliance.umich.edu/human-subjects), provides objective analysis and evaluation of human subjects research compliance for investigator research studies, units of the HRPP and the HRPP as a whole.

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*[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 18-Sep-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.

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1. **ROLES AND RESPONSIBILITIES**

**Principal Investigator**

An individual filling the role of Principal Investigator (PI) is responsible for the following activities:

* Understands and adheres to the research protocol, regulatory, institutional, and Good Clinical Practice guidelines that define compliance and non-compliance
* Manages and oversees the conduct of clinical trials, including the documentation and reporting of noncompliance to oversight and/or regulatory bodies, as appropriate
* Creates processes and procedures to document non-compliance
* Communicates with the IRBMED, OHRCR and other applicable entities in the case of noncompliance
* Responds to any reports of noncompliance made by study staff, monitors, auditors, Co-Investigators, vendors, sponsors, or research subjects
* Educates study staff and research subjects in order to prevent continuing non-compliance
* Oversees the termination of a clinical research site or the clinical trial for reasons of continuing noncompliance, when appropriate

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

**Study Coordinator(s)/Designee**

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

* Understands and adheres to the research protocol, regulatory, institutional, and Good Clinical Practice guidelines that define compliance and non-compliance
* Documents noncompliance in an accurate and time-sensitive manner
* Reports identified noncompliance to the PI
* Seeks to minimize the re-occurrence of protocol deviations and other sources of non-compliance through process improvements, additional training, etc.

(**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**

**Protocol Noncompliance**

*[Describe the process for communicating, documenting, and reporting identified protocol noncompliance. This may include processes for (re)education of study staff and participants, completion of protocol deviation records, and reporting to Sponsor, IRB and/or other oversight committees.]*

**Standard Operating Procedure (SOP) Noncompliance**

*[Describe the process for communicating, documenting, and reporting identified noncompliance with site SOPs. This may include processes for (re)education of staff, completion of a corrective action plan, and/or amending current SOPs.]*

**Escalation of Identified Noncompliance Issues**

*[Describe the process for escalating identified continuing noncompliance and serious noncompliance. This may include documentation, remediation, and reporting, to the appropriate study team member, regulatory bodies, etc.]*

**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 - CFR - Code of Federal Regulations Title 21 Subpart C -- IRB Functions and Operations:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56&showFR=1&subpartNode=21:1.0.1.1.22.3>

International Conference on Harmonisation (ICH):

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

ICH GCP – Compliance with Protocol:

http://ichgcp.net/45-compliance-with-protocol

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

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

University of Michigan - Operations Manual - Quality Assurance and Research Compliance:

<http://research-compliance.umich.edu/operations-manual-quality-assurance-and-research-compliance>

University of Michigan - Policy Statement on the Integrity of Scholarship and Procedures for Investigating Allegations of Misconduct in the Pursuit of Scholarship and Research:

<http://spg.umich.edu/policy/303.03>

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*[Optional: Insert any additional SOP references]*

1. **APPENDICES**

(**MANDATORY LANGUAGE**)

*[Optional: Insert any additional SOP appendices]*