1. PURPOSE

The purpose of this procedure is for handling audit findings and allegations of noncompliance and determining whether the noncompliance is serious and/or continuing. The procedure applies to all Avera Principal Investigators (PIs) and research personnel who conduct research involving human subjects as well as Avera designees responsible for the oversight of human subject research.

2. REPORTING NONCOMPLIANCE

An allegation of noncompliance occurs when information of suspected noncompliance comes to the attention of the IRB. All research personnel are required to conduct research in accordance with the approved protocol, federal regulations, state law, and Avera policy. Failure to do so constitutes noncompliance in the research endeavor, irrespective of the magnitude or intention. Research personnel, Avera Personnel or entities responsible for the oversight of human research who believe in good faith that they are aware of an instance of serious noncompliance are required to report such incidents to the DHSP/IRB.

Reports and allegations of serious noncompliance must be reported to IRB Staff as soon as possible. Reports of noncompliance involving the conduct of the IRB or their staff should be reported to the Executive Director of Research Compliance, if appropriate, or to the Institutional Official.

3. DEFINITIONS

Minor Protocol Deviation: Generally do not have a major impact on subject welfare or data integrity. Examples of a protocol deviation may include:

- Scheduling a required procedure outside of the time frame specified in the protocol
- Failure of subject to return study medication; or
- Implementation of unapproved recruitment procedure

Major Protocol Deviation: Affect a human subject's rights, safety or well-being or integrity of the data being collected. It may also affect the primary safety or efficacy endpoints of the study. Examples are:

- Enrolling human subject who did not meet entry criteria without prior permission
- Failing to obtain informed consent prior to any study-related procedures; or
- Failure to treat human subject's according to protocol procedures that specifically relate to primary safety or efficacy endpoints.

Minor Noncompliance: An occasional instance of noncompliance that is typically administrative in nature and does not affect the rights and welfare of human subject's or put participants at risk of harm.

Noncompliance: Failure to comply with federal regulations, Avera IRB policies, or the approved study protocol. Noncompliance may be serious, continuing, neither, or both. Noncompliance may result from the action of the human subject, PI, or staff. It may or may not impact the rights and welfare of the human subject or others, or the integrity of the study. Complaints or reports of noncompliance from someone other than the research PI are handled as allegations of noncompliance until such time that the report is validated or dismissed.

Serious Noncompliance: An action or omission taken by a researcher that could be seen as compromising the rights and/or welfare of the human subject's. It also may be an action or omission taken by a researcher that materially increases risk or results in substantial harm to human subject's or others.

The following instances will always be determined as serious noncompliance:

- Expedited or Full IRB level research conducted without IRB approval or without appropriate informed consent.
- Substantive modifications to IRB approved research without IRB approval.

Continuing Noncompliance: Noncompliance that occurs repeatedly and suggests a pattern or an underlying problem. It may occur due to a lack of knowledge (unintentional) or due to a deliberate choice to ignore regulations or determinations of the IRB (intentional).

4. PROCEDURES

4.1 Determination of Protocol Deviation or Noncompliance

4.1.1 Categorize. The finding will be initially screened to see if it appears to be major or serious and/or continuing. If more information is needed before this ruling can be made, there may be an investigation.

4.1.2 Potentially Major Protocol Deviations or Serious or Continuing Noncompliance.

a. The IRB Manager notifies the Chair(s) and Executive Director of Research Compliance. The study may be suspended or restrictions may be imposed immediately.
b. The researcher must respond with a corrective and preventive action plan.
c. The audit finding, determination, and corrective action plan are presented to the IRB.
d. The IRB votes on the determination and adequacy of corrective action plan.
e. If corrective action plan is not approved, the researcher will be asked for revisions.
f. Executive Director will monitor approved corrective and preventive action plan.
g. Relevant parties such as the department chair, Institutional Official, funding agency, other IRBs, other involved institutions, FDA, and/or OHRP, may be notified as appropriate.

4.1.3 Minor Protocol Deviations and Minor Noncompliance.

Since minor protocol deviations and minor noncompliance do not affect the rights and welfare of human subject's, or put participants at risk of harm, they do not need to be reported to the IRB.

4.2 Allegation of Noncompliance

4.2.1 Receipt of Allegation. Allegations may be accepted verbally or in writing. If verbally, the recipient should take care to record all relevant information and request a contact number for follow-up, unless the person desires to remain anonymous. The recipient should inform the caller that the matter will be investigated to the extent possible, given the information provided. The caller should be asked for any available evidence that will facilitate an investigation. It is permissible to advise the caller to provide additional information at a

later date if new information becomes available or if the caller remembers details that were not presented originally.

4.2.2 Notification of Allegation. The Manager will notify the Executive Director of Research Compliance, IRB Chair, Institutional Official, as well as the researcher.

4.2.3 Conduct an Investigation. If deemed necessary, the allegation will be investigated. The related study may be suspended or restrictions may be imposed while the investigation is underway. If noncompliance is found, the Manager will follow the process described in section 4 of this SOP.

5. CORRECTIVE AND PREVENTIVE ACTION PLAN

Included Elements. If an action plan is necessary, the following items may be considered:

1. Measurable and accomplishable action items.
2. An achievable deadline.
3. An individual accountable for accomplishing each action item.
4. Plan for preventing reoccurrence

Examples:

1. Suspend enrollment or all research procedures for specific study in question, in accordance with SOP on Suspension and Termination of IRB approval.
2. Termination of the research, in accordance with SOP on Suspension and Termination of IRB approval.
3. Audit all or some of the researcher's active protocols.
4. Modify the protocol.
5. Modify the information disclosed during the informed consent process.
6. Provide additional information to past participants.
7. Require that current participants re-consent to participation.
8. Provide information to current participants whenever such information might relate to their willingness to continue in the study.
9. Monitor the consent process.

6. APPEAL PROCESS

The researcher may appeal the IRB determination of serious noncompliance and the associated corrective action plan. To do so, a written justification must be submitted to the Manager for consideration. The researcher will be invited to come to the upcoming IRB meeting to present their appeal.

7. ROLES AND RESPONSIBILITIES

IRB Staff are responsible for the investigation of reports of non-compliance.

IRB Members are responsible for the review of reports of investigation of non-compliance and determination of actions needed to be taken by the IRB and PI.

8. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108(b)(2), 56.113

45 CFR 46

REVISION HISTORY

Revision Number	Version Date	Approved By, Date Approved
02	1/28/2019	Avera Institutional Official, 3/19/2019
• Moved the Protocol Deviation definition to this SOP #407 • Serious noncompliance must be reported to IRB, but minor protocol deviations and minor noncompliance does not need to be reported, since they do not affect the rights and welfare of human subject's or put them at risk of harm. • Removed the references to "Protocol Violations", as that is not a term used by OHRP or the FDA. • Updated applicable regulations • Removed section titled Procedures Employed to Implement This Policy with individual tasks and who is responsible for each item.		
01	August 2016	Director HSRP / August 2016