1. PURPOSE

This procedure describes what the IRB requires of a PI in the conduct of research, whether it is single site or multi-site.

2. PROCEDURE

It is the PI's responsibility to keep the IRB informed of unexpected, protocol-related, serious unanticipated problems (UP's), major protocol deviations, and other pertinent findings that could affect the risk/benefit ratio of the research. A PI is responsible for the accurate documentation, investigation and follow-up of all possible study related adverse events. PIs are also responsible for informing the study sponsors of any unanticipated or serious adverse events and other items as detailed in each individual protocol as appropriate.

3. SPECIFC PROCEDURES

3.1 IRB Review of Research

All human subjects research that is conducted by or under the direction of any Avera employee, staff, resident/student, or affiliate of Avera in connection with his or her Avera responsibilities must be reviewed by an IRB. PI's play a crucial role in protecting the rights and welfare of human subjects and are responsible for carrying out sound ethical research consistent with research plans approved by the IRB.

3.2 PI Expectations

Along with meeting the specific requirements of a particular research study, investigators are responsible for ongoing requirements in the conduct of approved research that include:

- obtaining prior approval from the IRB for any modifications of the previously approved research, including modifications to the informed consent process and document, except those necessary to eliminate apparent immediate hazards to human subjects;
- ensuring that progress reports and requests for continuing review and approval are submitted to the IRB in accordance with the procedures of the IRB;
- providing to the IRB prompt reports of any unanticipated problems involving risks to human subjects or others;
- providing to the IRB prompt reports of serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB; and
- keeping certain records as required by the HHS regulations or FDA regulations.

In addition to the above listed requirements, Avera also expects the PI's to:

- Disclose any COI (financial or other) that may affect the relationship with the research participant or the outcome of the research;
- Have sufficient time to conduct and complete the research;
- Ensure that all persons assisting in the research are adequately trained and informed about the protocol;
- Consider whether other procedures involving less risk are more appropriate when designing the research and will employ sound scientific design in the conduct of research;
- Minimize risk to the participant;

- Monitor participants for potential harm and take steps to minimize or lessen those harms when possible;
- Modify the research design to mitigate potential injuries in on-going research;
- Equitably recruit and select participants for the research;
- Quickly respond to requests of information or complaints;
- Keep current on policies and procedures that affect human subject protections;
- Seek guidance from IRB or other areas as appropriate; and
- Maintain research records, such as signed and dated informed consent documents, correspondence with IRB, supporting data, and any medical records associated with the research.

3.3 Informed Consent

The PI must obtain and document informed consent from human subjects prior to their participation in the research, unless these requirements have been waived by the IRB. The PI must use the informed consent document approved by the IRB. The IRB approved informed consent will have a date stamp approval which is located in the upper right-hand corner of the informed consent document. PI must follow federal guidelines and Avera IRB policy for obtaining informed consent.

3.4 Reports of Unanticipated Problems Involving Risks to Participants or Others

Reporting is required of all unanticipated problems. Please refer to IRB SOP 410 for details on this requirement.

3.5 Changes in Approved Research/Amendments

Changes in approved research during the period for which approval has already been given may not be initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to human subjects. Please refer to IRB SOP 403 for details on this requirement.

3.6 Continuations/Renewals and Project Closure

Continuations: The length of time approval is given to a research protocol will be no more than one year, and is dependent on the risk involved with the research. Please refer to IRB SOP 404 for details on this requirement.

Project Closure: All studies need to be closed once completed. Please refer to IRB SOP 405 for details on this requirement.

3.7 Resident/Student-Conducted Research

Activities that meet the definition of research with human subjects and that are conducted by residents/students for a class project or for work toward a degree must be reviewed by the IRB.

3.8 Education Requirement (CITI Human Subject Training)

It is an expectation that PI and key research personnel understand and apply their obligations to protect the rights and welfare of human subjects participating in research projects. In order to ensure that the minimum requirements are covered, all PIs, including project directors, advisors, key personnel, research staff, personnel conducting informed consent, and residents/student PIs, conducting research are required to complete CITI training. The following is the CITI training requirements per Avera SOP 300:

- For Full IRB or Expedited Reviews: CITI training with affiliation thru Avera Research Institute for PI and all research staff (Human Subjects Research [HSR] required modules for everyone, AND Good Clinical Practice [GCP] required modules for FDA-regulated studies).
- For Exempt research: CITI training with affiliation thru Avera Research Institute for PI and all research staff (Human Subjects Research [HSR] required modules for everyone)

Key personnel are defined as persons in contact with the human subjects or persons who have access to identifiable data. The CITI training must be completed before final IRB submission, and is good for three (3) years.

3.9 PI Qualifications for FDA-Regulated Studies

There are variances in who an IRB may allow to be the PI of FDA regulated studies.

- 21 CFR 812.43 (a): A sponsor shall select investigators qualified by training and experience to investigate the device.
- 21 CFR 312.53 (a): A sponsor shall select only investigators qualified by training and experience as appropriate experts to investigate the drug.
- FDA has no written guidance on whether a non-physician can serve as PI.

So although the FDA does not regulate whether the PI has to be a physician, Good Clinical Practice (GCP) does seem to suggest a higher standard. Although not specifically requiring a medical degree, GCP talks about medical decisions and qualified physicians.

- ICH GCP 4.1.1: The PI should be qualified by education, training and experience to assume responsibility for the proper conduct of the trial.
- ICH GCP 2.7: The medical care given to, and medical decisions made on behalf of, human subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
- ICH GCP 4.3.1: A qualified physician, who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical decisions.

Effective with v2.0 of this SOP (#800), for FDA-regulated studies involving drug or device, the PI must be a physician. All other investigators can only perform delegated tasks within their scope of practice for their licensure.

3.10 Record Keeping

It is the responsibility of the PI to maintain records of:

- Copies of all submissions, approvals and correspondence with the IRB;
- IRB stamped consent document(s) (all versions);
- Signed informed consent documents;
- Protocols and amendments (all versions); and
- Any other documentation requested by sponsor (for funded research).

3.11 Finder's Fees and Bonus Payments

Finder's Fees: PI and research staff shall not accept payments in exchange for referrals of potential participants.

Finder's fees pose a potential COI for the conduct of the research and, therefore, are prohibited. Faculty, staff, students, and all others conducting human research under the purview of Avera are strictly prohibited from offering or receiving any finder's fee or other inducement, in cash or in kind, for the purpose of referring patients as candidates for participation in research.

Likewise, no individual or organization conducting human research under the auspices of Avera may receive "bonus payments" from sponsors that are tied to the rate or timing of human subject enrollment. Examples are; an additional payment of $5,000 to sites if they can recruit an additional five (5) participants in a week, or additional payment to sites that reach their recruitment goals.

4. RESPONSIBILITY

IRB staff is responsible for tracking PI compliance with IRB requirements stipulated during the IRB's review of the PI's research, and for engaging appropriate PI sanctions when PIs are not in compliance with IRB requirements.

Chair (or designee) is responsible for facilitating PI compliance with IRB requirements through his/her management of IRB deliberations, and providing PI clear guidelines pertaining to that compliance through IRB communications to the PI.

IRB staff is responsible for checking if PIs have completed the CITI training.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109, 56.111, 21 CFR 54
45 CFR 46.109, 46.111, 46.116 46.117
21 CFR 812.43
21 CFR 312.53

6. REFERENCED DOCUMENTS

IRB SOP 403, 404, 405, 410

REVISION HISTORY

Revision Number	Version Date	Approved By	Date Approved
2.0	8/20/2020	Avera Institutional Official	9/22/2020
• Updated specific OHRP requirements for PI's, as it was noted that some were missing. • Referred to specific IRB SOPs that were much more in-depth with IRB requirements. • Updated the required CITI training modules. • Clarified that for FDA Regulated studies, the PI for Avera must be a physician, with an effective date of the approval of this SOP. • Updated applicable regulations. • Other administrative updates.			
1.0	August 2016	Director HSRP / August 2016	