1. PURPOSE

This procedure describes the requirements for obtaining informed consent and documentation of informed consent.

2. PROCEDURE

Informed consent must be legally effective and prospectively obtained. Except as described in SOP-701, Waivers of Informed Consent, no PI may involve a human subject as a research subject unless he or she has obtained informed consent from the human subject or the human subject's legally authorized representative (LAR). Informed consent shall be sought only under circumstances that provide the prospective human subject or the LAR sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence.

The informed consent of a human subject is a privilege freely granted by a human subject. He or she is under no obligation to participate. Furthermore, while obtaining the signature of a human subject is an event, obtaining informed consent is a process that leads to the signature and that is to be continued throughout the research, as may be required by respect for human subjects.

Unless waived by the IRB, the IRB requires documentation of informed consent by use of a written informed consent (including in an electronic format) approved by the IRB and signed and dated (including electronically signed and dated) by the subject or the subject's LAR. In studies involving children, the LAR is the parent or court-appointed guardian. Specific procedures for documentation of informed consent are covered in SOP-702.

2.1 Legally Authorized Representative (LAR)

In studies involving cognitively impaired adults, the LAR is a designated proxy (such as a durable power of attorney for health care), court-appointed guardian, or next-of-kin, in that order.
In this procedure, “human subject or LAR” means the human subject when the human subject is an adult capable of providing consent, or an LAR when the human subject is an adult unable to give informed consent, or one or both biologic or adoptive parents when the human subject is a child or in the absence of a parent, a person authorized under applicable law to consent on behalf of the child to the child’s general medical care.

3. SPECIFIC PROCEDURES

3.1 Informed Consent Document:

An informed consent document is one that embodies the elements of informed consent described in 21 CFR 50.25 and 45 CFR 46.116(a) and (b) and (c), as applicable. The informed consent may be read to the human subject or the human subject's LAR; but, in any event, the PI (or delegated individual) shall give either the human subject or the human subject’s LAR adequate opportunity to read and reflect upon it before it is signed.

The human subject or the human subject’s LAR signs and dates the informed consent document. An electronic signature will be accepted just as a wet signature is accepted. The human subject must be given a copy of the informed consent document.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the human subject; (b) a short form written informed consent form with oral presentation; or (c) in limited circumstances, waiver of signed written informed consent form.

3.1.1 Short Forms

Regulations permit oral presentation of informed consent information in conjunction with a short form written informed consent document (stating that the elements of informed consent have been presented orally) and a written summary of what is presented orally. A witness to the oral presentation is required, and the human subject must be given copies of the short form document (in a language they can understand) and the summary.

If the informed consent process will be documented in writing with the short form of informed consent documentation:

1. Obtain the current IRB approved short informed consent form and summary. Note that the IRB-approved English language informed consent document may serve as the summary.
2. Verify that the short informed consent form is in a language understandable to the human subject or human subject's LAR.
3. Obtain the services of an *interpreter* fluent in both English and the language understood by the human subject or human subject's LAR. The interpreter may be a member of the research team. Utilizing a family member or friend of the human subject or human subject's LAR as the interpreter is discouraged, but may be used.
4. Obtain the services of an *impartial witness* who is fluent in both English and the language spoken by the human subject or human subject's LAR to be present during the entire informed consent discussion. *The impartial witness and the interpreter may be the same person*. A witness is required to be in attendance, and to attest that the information in the short informed consent form, summary, and any other information provided was accurately explained to, and apparently understood by, the human subject or human subject's LAR, and that informed consent was freely given. The witness may be a family member or friend. The witness may not be a person involved in the design, conduct, or reporting of the research study.
5. Through the interpreter, translate the summary (not the short informed consent form) to the human subject or human subject's LAR. Explain the details in such a way that the human subject or human subject's LAR understand what it would be like to take part in the research study. When necessary, provide a different or simpler explanation to make the information understandable.
6. Have the human subject or human subject's LAR read the short informed consent form, or have the interpreter read the short informed consent form to the human subject or human subject's LAR.
7. Invite and answer the human subject or human subject's LAR's questions.
8. Give the human subject or human subject's LAR time to discuss taking part in the research study with family members, friends and other care providers as appropriate.
9. Invite and encourage the human subject or human subject's LAR to take the written information home to consider the information and discuss the decision with family members and others before making a decision.

10. Ask the human subject or human subject's LAR questions to determine whether all of the following are true, and if not, either continue the explanation or determine that the human subject or human subject's LAR is incapable of providing informed consent:
    a. The human subject or human subject's LAR understands the information provided.
    b. The human subject or human subject's LAR does not feel pressured by time or other factors to make a decision.
    c. The human subject or human subject's LAR understands that there is a voluntary choice to make.
    d. The human subject or human subject's LAR is capable of making and communicating an informed choice.
11. If the human subject or human subject's LAR has questions about treatments or compensation for injury, provide factual information and avoid statements that imply that compensation or treatment is never available.
12. Once a human subject or human subject's LAR indicates that he or she does not want to take part in the research study, this process stops.
13. If the human subject or human subject's LAR agrees to take part in the research study, proceed with the documentation of the informed consent process.

    To **DOCUMENT** the informed consent process in writing, signatures should be obtained as follows:
    1) The short informed consent form should be signed by the human subject or human subject's LAR, which is written in a language that they can read and understand.
    2) The summary should be signed by the person obtaining informed consent.
    3) The short informed consent form and the summary should be signed by the witness. When the person obtaining informed consent is assisted by a translator, the translator may serve as the witness.

    Provide a copy of the signed and dated short informed consent form and a copy of the signed and dated summary to the human subject or human subject's LAR. This may be accomplished either by making photocopies or by having the above individuals sign and date two copies of the short informed consent form and summary.

    The IRB must receive all foreign language versions of the short informed consent form as a condition of approval. Expedited review of these versions is acceptable if the full English language informed consent form has already been approved by the IRB.

3.2 Requirements for Informed Consent or Parental Permission

The IRB has the responsibility for approving a consent form or parental permission form unless waived in accordance with 45 CFR 46.116(d) under pre-2018 Requirements, and 45 CFR 46.116(f) under 2018 Requirements.

Informed consent must be documented by the use of a written informed consent form (including in an electronic format) approved by the IRB unless documentation is waived by the IRB as provided in 45 CFR

46.109(c), 46.117, and, when applicable, 21 CFR 56.109(c). A copy of the informed consent form is provided to the human subject or human subject's LAR.

The informed consent form must be a written informed consent form that embodies the elements of informed consent detailed in section 3.3 and required by regulations.

The informed consent form must be written so that it does not include any exculpatory language through which the human subject or human subject's LAR is made to waive or appear to waive any of the human subject's legal rights; or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence as stated in 45 CFR 46.116 and 21 CFR 50.20.

3.3 Elements of Informed Consent

Elements of informed consent include the following per 45 CFR 46.116(a) under pre-2018 Requirements, 45 CFR 46.116(b) under 2018 Requirements, and 21 CFR 50.25(a) for FDA-regulated studies:

1. Statement that the study involves research.
2. Explanation of the purposes of the research.
3. Expected duration of the human subject's participation in the research.
4. Description of the procedures to be followed.
5. Identification of any procedure that is experimental.
6. Description of any reasonably foreseeable risks or discomforts to the human subject.
7. Description of any benefits to the human subject or to others, which may reasonably be expected from the research.
8. Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the human subject.
9. Statement describing the extent, if any, to which confidentiality of records identifying the human subject will be maintained, and if applicable, a statement of the possibility that the FDA may inspect the records, if applicable.
10. For research involving more than minimal risk, an explanation as to whether any compensation is available if injury occurs, whether any medical treatments are available if injury occurs, and if so, what they consist of, or where further information can be obtained.
11. Explanation of whom to contact for answers to pertinent questions about the research, human subject's rights, and whom to contact in the event of a research-related injury to the human subject or if the human subject has concerns or complaints about the research.
12. Statement that participation is voluntary, that refusal to participate involves no penalty or loss of benefits to which the human subject is otherwise entitled, and that the human subject may discontinue participation at any time without penalty or loss of benefits to which the human subject is otherwise entitled.
13. For research that falls under 2018 Requirements (45 CFR 46.116(a)(5)), the following is required:
    a. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective human subject or human subject's LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.
    b. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide

lists of isolated facts, but rather facilitates the prospective human subject's or human subject's LAR's understanding of the reasons why one might or might not want to participate.

When appropriate, one or more of the following additional elements of information shall also be provided to each human subject per 45 CFR 46.116(b) under pre-2018 Requirements, 45 CFR 46.116(c) under 2018 Requirements for more than minimal Risk:

1. A statement that the human subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the human subject will or will not share in this commercial profit;
2. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to human subjects, and if so, under what conditions; and
3. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate genome or exome sequence of that specimen).
4. When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each human subject in informed consent forms and processes. The statement is: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Additional required elements for FDA-regulated studies as per 21 CFR 50.25(b):

1. Statement that the particular treatment or procedure may involve risks to the human subject (or to the unborn baby, if the subject is or may become pregnant) which are currently unforeseeable.
2. Anticipated circumstances under which the human subject's participation may be terminated by the PI without regard to the human subject's consent.
3. Any additional costs to the human subject that may result from participation in the research.
4. Consequence of a human subject's decision to withdraw from the research and procedures for orderly termination of participation by the human subject.
5. Statement that significant new findings developed during the course of the research, which may relate to the human subject's willingness to continue, will be provided to the human subject.
6. Approximate number of human subjects involved in the study.

3.4 Payment or Compensation

Payment or compensation to human subjects should not be considered a benefit, but a recruitment incentive. The compensation should not be such that it would be considered coercive or unduly influence human subjects to enroll into a study or stay in a study. All information concerning the compensation, including the amount and schedule of payments, should be included in the informed consent document. The compensation should not be contingent upon completion of the study, but should be prorated.

3.5 Reproductive Risks

Avera Facilities are guided by *Ethical and Religious Directives for Catholic Health Care Services.* In recognition of these principles the Avera IRB requires the following verbiage on informed consent documents that include sections on reproductive risks:

a. Females: Due to the unknown effects of this study's drugs/device on an unborn child, you understand that it is very important that you do not become pregnant during this study. Avoiding sexual activity (total abstinence) is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you must agree to use acceptable method(s) of preventing pregnancy while in this research study. Please discuss with your doctor the most appropriate method(s) of preventing pregnancy for you that also respects your cultural and religious values and traditions.

b. Males: Due to the unknown effects of this study's drugs/device on an unborn child, you understand the risk of birth defects if your partner becomes pregnant during this study. Avoiding sexual activity (total abstinence) is the only certain method to prevent pregnancy. However, if you choose to be sexually active, you must agree to use acceptable method(s) of preventing pregnancy while in this research study. Please discuss with your doctor the most appropriate method(s) of preventing pregnancy for you that also respects your cultural and religious values and traditions. Inform your study doctor if you think for any reason that your partner might be pregnant.

<u>Additional Protection(s) Preferred Language</u>

- Breastfeeding: If a mother is or plans to breastfeed, the following language should be included:

  Your study doctor will give you specific information for the treatment you will be taking regarding pregnancy prevention and breast feeding.
- For males – sperm donation:

  Please speak with your doctor if you have questions or concerns about sperm donation.
- Pregnancy testing: When pregnancy testing is mentioned in the informed consent form, you should specify that a *SERUM* pregnancy test be used and that it be completed as close to treatment initiation as possible.
- Fertility Preservation: If you wish to become pregnant or father a child in the future, please discuss fertility preservation options with your doctor before you begin participating in this study.

<u>Additional changes specific to Avera</u>:

- References to Unborn Baby: refer to *fetus* and *embryo* as "unborn baby" or "unborn child."
- Replace *birth control/contraception* with "pregnancy prevention."
- Delete references to specific methods of contraception:
  a. Oral contraceptives, birth control pills, hormonal contraception
  b. Contraceptive injectables and implants
  c. Barrier methods, including condoms, diaphragms, cervical caps

d. Intrauterine devices (IUD), intrauterine systems (IUS)
e. Spermicidals
f. Withdrawal

- Pregnancy prevention methods which may be mentioned:
  a. Natural family planning, including symptom method, symptom-thermal method, Creighton method
  b. Abstinence from sexual intercourse
  c. Patient or partner is sterile

3.6 Translations of Consent Documents into a Foreign Language

Translations of informed consent documents, if applicable, will be submitted for IRB approval and will be reviewed in an expedited manner. There are two options available to obtain approval of translated consent forms.

- Option #1: The IRB-approved informed consent form is translated by the sponsor or site and submitted to the IRB. The IRB will have a member or consultant fluent in the language of the consent review the translated document for accuracy. In his/her opinion it must match the English version.
  - If the IRB does not have a consultant available, the PI will need to obtain and pay for translation services.
- Option #2: The PI (or sponsor) may submit the most current IRB-approved version of the informed consent form to an IRB-approved, certified translator. A second translator may then back translate the informed consent form to the original English. Both original and back-translated informed consent form must be submitted, and a Certificate of Accuracy is preferred.

3.7 Observation of the Informed Consent Process

The IRB may observe the informed consent process in ongoing research, when appropriate. As part of the IRB oversight options, an IRB may require that a staff member, IRB member, or outside third party observe the informed consent process of human subjects to determine whether the informed consent process has been appropriately completed and documented.

An IRB may require that selected protocols have one or more informed consent process situations be observed. IRB considerations used to choose such protocols include:

- High risk studies.
- Studies that involve particularly complicated procedures or interventions.
- Studies involving vulnerable populations.
- Studies involving study staff with minimal experience in administrating informed consent to potential study participants.
- Other situations when the IRB has concerns that the informed consent process is not occurring in a manner consistent with applicable regulations.

3.8 Withdrawal from a Clinical Trial

The IRB considers the following issues regarding data retention when human subjects withdraw from a clinical trial:

- When a human subject withdraws from a study, the data collected on the human subject to the point of withdrawal remains part of the study database, and may not be removed. The informed consent document cannot give the human subject the option of having data removed.
- A researcher may ask a human subject who is withdrawing whether he/she wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the human subject should distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the human subject's information.
    - The researcher must obtain the human subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). The IRB must approve the consent document.
    - If a human subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access the human subject's medical record or other confidential records for purposes related to the study. However, a researcher may review study data related to the human subject when it was collected prior to the human subject's withdrawal from the study, and may consult public records, such as those records establishing survival status.

3.9 Informed Consent Procedures via Telephone, WebEx, Skype, or other Electronic Media

There may be situations when obtaining informed consent from human subjects over the **telephone, or by WebEx, Skype, or other electronic media** is appropriate. In these situations, the person obtaining informed consent must document that the informed consent process took place by making appropriate notation regarding the process in the proper files. **Before implementing either of the processes described below, the PI must first obtain appropriate IRB approval to do so.**

Informed consent may only be obtained via telephone or other electronic media process when written documentation of informed consent has been waived by the IRB. Alternatively, if human subjects will be signing the informed consent document after having discussed the research study with a member of the research team over the telephone (or other electronic media), a waiver of written documentation of the informed consent is not required. In this case, the person discussing the research study with the potential human subject should sign and date the informed consent document prior to mailing, emailing or faxing it to the potential human subject. Appropriate notation should be made in the human subject's records indicating that the process took place. Once the human subject receives, signs, and returns the informed consent document to the study site, the document should again be signed and dated by the appropriate member of the research team who receives the document.

3.10 Use of Fax, Email or Mail to Document Informed Consent

There may also be situations when obtaining informed consent from human subjects by fax, mail or email is appropriate. This is acceptable in situations where the informed consent process has already

been appropriately conducted in person. For example, it is acceptable for the informed consent discussion to initially take place in person, and then allow the potential human subject time to take the informed consent form home in order to consider participation. Later on, the human subject may sign and fax, email or mail the informed consent form back to the research site.
In this case, the person obtaining informed consent should sign the informed consent form and make appropriate notes to the human subject's record upon completion of the informed consent discussion. The appropriate recipient of the signed original informed consent form should sign and date it, file it with the faxed, emailed or mailed copy, and make appropriate notes to the human subject's record. The notes to file coinciding with the dates and signatures on the informed consent forms provide the source documentation that confirm and explain how the informed consent process occurred.

The IRB may also approve a process that allows the informed consent form to be delivered by mail, email or fax to the potential human subject or the potential human subject's LAR and to conduct the informed consent discussion by telephone when the human subject or human subject's LAR can read the informed consent form as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

4. RESPONSIBILITY

Primary and Secondary (when applicable) Reviewers are responsible for carefully reviewing all incoming informed consent documents and for communicating revisions at the IRB meeting, when appropriate

IRB members are responsible for reviewing informed consent documents prior to the IRB meeting.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50
21 CFR 56.109
45 CFR 46.116; 46.117; 46.109

6. REFERENCED DOCUMENTS

SOP 701 – Waivers of Informed Consent
SOP 702 – Documentation of Informed Consent

Revision Number	Version Date	Approved By	Date Approved
2.0	6/29/2020	Avera Institutional Official	7/10/2020
• Updated the steps to follow for using a Short Form. • Updated the language used at Avera regarding reproductive risks, as guided by *Ethical and Religious Directives for Catholic Health Care Services.* • Updated Regulations, per updates to 2018 Common Rule. • Listed out the Elements of Informed Consent, that must be in the informed consent form. • Other administrative edits.			
1.0	August 2016	Director HSRP / August 2016	