1. PURPOSE

This procedure describes the process for continuing review of approved research prior to the expiration of the IRB approval period.

2. PROCEDURE

The IRB conducts continuing review (renewal) of research taking place within its jurisdiction at intervals appropriate to the degree of risk. Research projects must be reviewed and re-approved by the Avera IRB prior to the study's expiration date, unless the study qualifies under the 2018 Common Rule Revision [as noted in 45 CFR 46.109(f)] and does not need to be submitted for annual continuation/renewal.

3. SPECIFIC PROCEDURES

3.1 Interval for Review for Purposes of Renewal

The IRB must conduct continuing review of protocols for purposes of renewal of the IRB approval period, at intervals appropriate to the degree of risk. For studies that qualify for expedited review under the 2018 Common Rule Revision and were approved initially on or after 1/21/19, or were approved before 1/21/19 and were transitioned to the 2018 Common Rule Revision, the study does not need to be submitted for annual continuation/renewal. If the study was approved initially before 1/21/19 and was *not* transitioned, then the study will need to be submitted for annual continuation/renewal.

For all FDA-regulated studies, and studies which do not fall under the 2018 Common Rule Revision, continuing review must occur not less than once per year. "Not less than once per year" means that the research study must be reviewed before the one year anniversary of the previous IRB review date, even though the research study activity may not have begun until sometime after the date of IRB approval.

PIs or qualified designees are required to submit a periodic report prior to the expiration of the study or as specified by the IRB. The report should be filed 40 days before the study approval period ends.

3.2 Extensions of Approval Period

There is no grace period for extending continuation of research related activities beyond the study's expiration date. If Continuing Review submissions and other requested progress reports are not received by the IRB as required, the PI must suspend the study and study enrollment until reports are reviewed and continuation is approved.

If the PI is in communication with the IRB, and the Continuing Review submission or other information is forthcoming, and in the opinion of the IRB, human subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time, if the IRB staff approves of such on a short-term interim basis. New human subjects cannot be enrolled during this time. Prospective research data cannot be collected, and procedures performed only for the purposes of the research study may not be performed until a Continuing Review submission is reviewed and approved.

3.3 Criteria for Continuation/Renewal

Research study activities initially reviewed by full Board review must be reviewed by the full Board at continuation, unless:

- The study has been modified and is now eligible for expedited review as defined in the regulations (e.g., change in risk to minimal); or
- The study meets one of the following expedited review criteria:
  1. The research at this site is permanently closed to the enrollment of new participants; all participants at this site have completed all research-related interventions; and the research at this site remains active only for long-term follow-up of participants; **or**
  2. No participants have ever been enrolled at this site and no additional risks have been identified; **or**
  3. The remaining research activities at this site are limited to data analysis.

Research activities that were originally reviewed using expedited criteria may receive continuing review on an expedited basis, unless the research activities no longer meet the expedited criteria for review and approval.

Research activities that had previously met criteria for expedited review may change with the review and approval of amendments, such that full board IRB review would be required at the time of continuing review (e.g., risk has changed to be greater than minimal).
When conducting research under an expedited review procedure, the Chair or designee conducts the review on behalf of the IRB using the same criteria for continuation as stated in section 3.4 of this procedure. If the reviewer feels that there has been a change to the risks or benefits, he or she may refer the study to the full IRB for review.

3.4 Continuation Materials and Review
Continuing review must be substantive and meaningful. When considering whether or not to renew a study, the IRB revisits the same criteria for approval used to grant initial approval. The reviewer(s) have access to the IRB study file and all documents submitted by the PI, including any previous modifications that have been approved by the IRB. (See SOP 300 for submission requirements for continuing review.) The reviewer(s) use a checklist to determine if the study meets the criteria for renewal. The status report on the progress of the research study should include:

- The number of subjects enrolled, withdrew, on active treatment, etc.
- A summary since the last IRB review of:
  - Adverse events, SAE's, adverse outcomes experienced by participants, and Unanticipated Problems
  - Participant withdrawals
  - The reason for withdrawals
  - Complaints about the research
  - Amendments or modifications
  - Any relevant recent literature
- The researcher's current risk-potential benefit assessment based on study results.

3.5 Primary and Secondary Reviewers
At continuing review, the Primary and Secondary Reviewer system is typically used for full IRB reviews. The Primary and Secondary Reviewers review, in depth, the complete protocol including any protocol

modifications previously approved by the IRB. A single Primary reviewer system is used for Expedited Reviews.

3.6 Possible Outcomes of Review for Continuation

As an outcome of continuation review, the IRB may authorize continuation of the research, require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol.

Appropriate continuing review intervals are addressed with each review conducted by the IRB. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:

- Involvement of vulnerable populations.
- Involvement of recombinant DNA or other types of gene transfer protocols.
- Use of waiver of informed consent procedures.
- Research for which participants would be exposed to additional risks, e.g., breach of confidentiality, phase I studies, disproportionate number or severity of adverse events, and
- Previous suspensions of the research due to compliance, record-keeping, or other concerns.

Any changes required to obtain continued renewal approval shall be provided to the PI by the IRB staff.

3.7 Date of Continuing Review Approval

If the IRB grants a one year approval of the continuation, the date of continuation will be determined by the date the research study was approved by the convened IRB. If the study is reviewed by expedited review, the approval date will be determined by the date the study is approved.

3.8 Humanitarian Device Exemption – Renewal

A Humanitarian Device Exemption (HDE) is an application that is similar to a pre-market approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD). As defined in the Federal Food, Drug, and Cosmetic Act (the Act), a HUD is a device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or is manifested in fewer than 4,000 individuals in the United States per year.

IRBs are responsible for initial as well as continuing review of the HUD. For continuing review, IRBs may use the expedited review procedures provided it meets the criteria for expedited review as per 21 CFR part 56.110 and 56.111, unless the IRB determines that full IRB review should be performed. The FDA agency believes that the expedited review procedures are appropriate for continuing review since the initial review would have been performed by the full IRB and use of a HUD within its approved labeling does not constitute research. Please refer to IRB SOP-505 Humanitarian Use Device for further requirements.

4. RESPONSIBILITY

IRB Staff are responsible for establishing and implementing processes for making research study renewal decisions.

Chair, designee, IRB members are responsible for the review of continuations.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108, 111
21 CFR 814, Subpart H – Humanitarian Use Devices
21 CFR Part 812 Subpart D – Investigational Device Exemptions IRB Review and Approval
21 CFR Part 312.66 – Assurance of IRB Review
45 CFR 46.111
45 CFR 46.109

Revision Number	Version Date	Approved By, Date Approved
2.0	6/7/2019	Avera Institutional Official 8/8/19
• Added in language regarding the updated Common Rule, and when studies qualify that they do not need to be submitted for annual continuation. • Other minor administrative changes.		
1.0	August 2016	Director HSRP / August 2016