Purpose:

The IRB conducts continuing review for each study protocol to ensure the ongoing protection of the rights and welfare of research subjects.

Responsible Personnel:

Background:

Continuing review of human subjects research will occur at intervals appropriate to the degree of risk, but not less frequently than once a year. The IRB applies the same criteria for approval of continuing review as it does for initial applications. In accordance with IRB SOP 2.0 Section 2.7, the Committee may set approval periods and requirements for continuing review at intervals of less than one year or at intervals dependent on subject accrual or at any time when unanticipated problems are encountered. The IRB has the discretion to increase the frequency of review if new information negatively impacts the risk/benefit ratio or if the Committee is notified of a complaint or alleged compliance violation. Once the study is eligible for expedited continuing review, the review interval may revert to one-year.

Regulation and Guideline Reference(s):

45 CFR 46.109
21 CFR 56.109
45 CFR 46.110
45 CFR 46.111
21 CFR 56.111
45 CFR 46.115
6.1 General Requirements for Continuing Review

I. This standard operating procedure applies to research conducted under the KUMC Federalwide Assurance #00003411. It also applies to all research that is greater than minimal risk, regardless of funding source.

II. When required by federal regulations, the IRB conducts continuing review for approved study protocols to ensure the ongoing protection of the rights and welfare of research subjects.
   A. For non-exempt research approved before January 21, 2019, continuing review will occur at annual intervals until the closure of the study or until the study is transitioned to review under the Revised Common Rule.
   B. For research approved after January 21, 2019, the IRB's continuing review of research will conform to the Revised Common Rule and FDA regulations when applicable. Continuing review will occur at intervals appropriate to the degree of risk, but not less frequently than once a year.

III. As of January 21, 2019, continuing review will not be required for newly-approved or transitioned research described in this section 6.1 III below, unless the IRB documents its rationale. Under the Revised Common Rule, continuing review would not be required for research that:
   A. Is eligible for expedited review
   B. Is approved by limited IRB review:
      1. Data analysis, including analysis of identifiable private information or identifiable biospecimens and/or
      2. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care and not specifically for research purposes.

IV. Federal regulations allow exceptions to the above categories. At its discretion, the KUMC IRB may determine and document rationale for continuing review when the research is (1) associated with an investigator or institutional conflict of interest; (2) multi-site research for which the KUMC IRB is the reviewing IRB; (3) associated with compliance concerns or other factors determined and documented by the IRB.

6.2 IRB Office Notifications

I. The electronic IRB system sends notifications to investigators 90, 60, 30, and 15 days prior to expiration. The online section of the Continuing Review submission provides a general status update. A Continuing Review Supplement, prepared by the investigator and uploaded to the submission, provides local information that allows the IRB to complete its review prior to the expiration date.

II. Once complete continuing review materials are submitted, a determination is made whether the continuing review is eligible for expedited review or if it should be scheduled for a convened meeting.
III. If expedited review is not applicable, the Continuing Review will be placed on the agenda for review at the next available meeting.

6.3 Continuing Review Submission Materials
I. The Continuing Review includes information on the status of the project, number of subjects, reportable events, complaints, numbers of withdrawals and reasons for withdrawals, relevant literature, significant new information, information about safety oversight, and oversight activities at non-KUMC sites, when applicable.

II. All previously approved documents are housed within the electronic system and available at the time of the continuing review. Most requests for continuation are submitted as a Continuing Review action. If personnel changes are requested at the time of the investigators submit a Modification/ Continuing Review for study personnel changes through the eIRB system. If protocol amendments or other changes are also being requested, they are submitted in the eIRB system as a separate modification. The Continuing Review request must be accompanied by a Continuing Review Supplement.

III. At the time of submission, a member of the IRB office staff will review the submission for completeness. If any required materials are missing, office staff will contact the investigator to obtain the missing information prior to assignment for review. If the staff notes that there are any submissions that are concurrent to the continuing review, those issues will be communicated to the primary reviewer.

IV. When required by regulation or institutional policy, review of ongoing research must occur prior to the study expiration date. If this does not occur, then the IRB follows section 6.7 below.

6.4 Continuing Review by the Convened Board
I. Continuing review is conducted by the convened board as required by the Revised Common Rule, by FDA regulations or as deemed necessary by the IRB as described in 6.1 above.

II. At each meeting, members may conduct continuing reviews of previously approved protocols. The reviews are designed to ensure that the rights and welfare of subjects continue to be protected. Continuing reviews include protocols that are determined to require more than annual review, as well as those with annual review requirements. In continuing review, the IRB ensures that the same standards as applied in the original review are still present (e.g., minimized risk, risks reasonable in relation to benefits, equitable selection, adequate informed consent process and documents, monitoring data to ensure subject safety, privacy protections, confidentiality protections, and appropriate safeguards for vulnerable populations).

III. Continuing review materials are available to IRB members along with all other review assignments, approximately 5 days prior to the meeting. One member is assigned as the primary reviewer for the continuing review. All previously approved documents are housed within the electronic system and available at the time of the continuing review. Most requests for continuation are submitted as a Continuing Review action. If personnel changes are requested at the time that investigators submit a Modification/ Continuing Review for study personnel changes through the eIRB system. If protocol amendments or other changes are also being requested, they are submitted in the eIRB system as a separate modification.

IV. The submission may include the following documents:
   A. Continuing Review Form, which includes a summary of changes since the last review:
   B. Currently approved protocol:
   C. Current informed consent document(s);
D. For studies being monitored by a data monitoring committee or data and safety monitoring board, all safety monitoring reports for the reporting period;

E. Any correspondence from the FDA;

F. Device accountability log, for device studies;

G. A copy of any FDA audits of sites under the auspices of the KUMC investigator;

H. The most recent FDA progress report, for studies in which the KUMC investigator holds the IND or IDE.

V. The remaining members who are scheduled to attend the meeting, and who do not act as a primary reviewer, have access to the above items via the eIRB system.

VI. Primary reviewers conduct an in-depth review of the provided materials. These reviewers should:

A. Examine the complete application submitted with the continuing review, to determine whether the protocol needs verification from sources other than the researchers that no material changes have occurred since the previous IRB review;

B. Consider if new or additional risks have been identified (e.g. unanticipated problems) that would require changes to the protocol, consent form, review frequency, etc.;

C. Consider if any new information may impact subjects' willingness to continue participation;

D. Report to the IRB Chair or IRB staff if it appears that the research is not being conducted in accordance with IRB requirements;

E. Confirm, in light of the above information, that the current consent is still accurate and complete;

F. Determine, in light of the above review, whether or not the study continues to meet federal criteria for approval;

G. Determine whether or not the continuing review interval should change.

VII. Each continuing review is separately discussed at the meeting. Any member who has a conflicting interest on the study leaves the room during discussion and voting.

VIII. At the meeting, the reviewer gives a summary of the study history since the last continuing review. The reviewer gives an evaluation of whether or not the study continues to meet federal criteria for approval.

IX. After discussion, the IRB determines whether the study continues to meet federal approval criteria and votes on one of the actions listed in section 6.6 below. The approval period is set, based upon the continuing review schedule determined by the Committee. Studies may be scheduled for Continuing Review more frequently than annually as discussed in IRB SOP 2.0 section 2.7.

X. In accordance with IRB SOP 2.0, the Committee may set approval periods and requirements for continuing review at intervals of less than one year or at intervals dependent on subject accrual or at any time when unanticipated problems are encountered. At the time of continuing review, the IRB has the discretion to increase the frequency of review if new information negatively impacts the risk/benefit ratio or if the Committee is notified of a complaint or alleged compliance violation. Conversely, research previously reviewed at intervals less than one year can be changed to annual review if supported by updated information about safety or appropriate compliance.

XI. If continuation is approved and enrollment is ongoing, the IRB staff will issue a new consent form with new approval and expiration dates. If the approval and expiration dates are the only changes, then re-consenting at continuing review is not required.
XII. Approval and expiration dates are calculated as follows:

A. Continuation approved at a convened meeting
   1. If the project is re-approved for continuation at a convened meeting, the approval date is the
case of the meeting.
   2. The expiration date is based on the date of the convened meeting (minus one day).
   3. For example, if the project is re-approved at a meeting on 10/1/2017, the approval period is 10/
   1/2017 – 9/30/2018 for an annual approval or 10/1/2017 - 3/31/2018 for a six month approval.

B. Continuation conditionally approved
   1. If the continuation is conditionally approved at a convened meeting, the approval date is the
case of the meeting.
   2. Unlike for initial reviews, the expiration date for continuing review is calculated from the date of
   the convened meeting (minus one day).
   3. For example, if the IRB conditionally approves a project on 10/1/2017, and the conditions are
   satisfied on 10/15/2017, then the approval period is 10/15/2017 - 9/30/2018 for an annual
   approval or 10/15/2017 - 3/31/2018 for a six month approval.

XIII. At the time of submission and review, the IRB has the discretion to require external verification that no
material changes have occurred since the previous review. External verification may be required when
the study is classified as high risk, when the investigator has previously failed to comply with IRB
requirements, when materials submitted for continuing review include unapproved modifications or
inconsistent information, or when the IRB has been informed of non-compliance by another source.
External verification can be arranged with the Quality Assurance Program or other components of the
Office of Compliance

XIV. If new issues arise during the course of the study that require additional expertise from outside the
committee, any member may request that the HRPP Director or IRB staff arrange a consultant for the
continuing review, as described in IRB SOP 2.0 section 2.8.

6.5 Expedited Continuing Review

I. HHS-regulated research that is greater than minimal risk must undergo continuing review at least
annually until it has progressed to the time points outlined above in 6.1.III. The continuing review for these
projects may be provided on an expedited basis if no subjects have been enrolled to date and no
additional risks have been identified.

II. All FDA-regulated research is subject to continuing review requirements. Unless the criteria below are
met, continuing review of FDA-regulated research will occur as outlined in 6.4 above. Continuing review
of FDA-regulated research may occur by expedited procedures when the research is:
   A. permanently closed to the enrollment of new subjects; all subjects have completed all research-
related interventions; and the research remains active only for long-term follow-up of subjects; or
   B. Where no subjects have been enrolled and no additional risks have been identified; or
   C. Where the remaining research activities are limited to data analysis.
   D. Where the study involves a humanitarian use device

III. Expedited continuing review will occur at least annually. Continuing review is no longer required once the
FDA-regulated research has progressed to the point of analyzing only data that meets HIPAA criteria for
de-identification.

IV. During pre-review, the IRB staff determines whether the continuing review qualifies for expedited review. If a project qualifies for expedited continuing review, the review may be conducted by the IRB Chairperson or by one or more qualified reviewers designated by the chairperson from among members of the IRB. A qualified IRB member means a current voting member or alternate voting member who has received training relative to the expedited review categories, and possesses the scientific or regulatory expertise needed to review the proposed research. The reviewers have ready access to the entire IRB file, which includes the complete protocol, consent form and all other documents that have been submitted to the IRB.

V. The IRB Chair or a qualified member(s) reviews the request for continuation to ensure compliance with current regulations and standards. Reviewers should:

A. Examine the complete application submitted with the continuing review, to determine whether the protocol needs verification from sources other than the researchers that no material changes have occurred since the previous IRB review;

B. Consider if new or additional risks have been identified (e.g. unanticipated problems) that would require changes to the protocol, consent form, review frequency, etc.;

C. Consider if any new information may impact subjects’ willingness to continue participation;

D. Report to the IRB Administrator, IRB Chair or HRPP Director if it appears that the research is not being conducted in accordance with IRB requirements;

E. Confirm, in light of the above information, that the current consent is still accurate and complete;

F. Determine, in light of the above review, whether or not the study continues to meet federal criteria for approval.

VI. The designated reviewer documents the review in the electronic IRB system.

A. If the research is re-approved without conditions, the approval date is the date of the designated review and the expiration date is one year minus one day from the approval date.

B. If the designated reviewer determined additional conditions must be met prior to re-approval, the approval is the date that the IRB staff confirm that all conditions from the designated reviewers are satisfied.

1. The expiration date is one year minus one day from the date of designated review.

2. For example, if the designated review occurred on 9/15/17, and the conditions were satisfied on 10/1/17, the approval period would be 10/1/17 – 9/14/18.

VII. If the research is approved for continuation through an expedited review procedure, the full committee is notified of the approval through the listing of expedited activities in the eIRB system.

6.6 IRB Actions on Continuing Review

I. The types of action possible at continuing review are listed below. Investigators should note that when the continuation is deferred or conditionally approved, the investigator must plan ahead to meet relevant deadlines to assure that the project's approval does not lapse.

A. Reviewed and Approved to Continue. The project is approved for continuation until the next expiration date.

B. Deferred-Additional Review by Committee Required. Continuation in this category is deferred
when the IRB requests substantive clarifications or modifications regarding the protocol or informed consent document(s) that are directly relevant to the federal criteria for human research approval (see SOP 2.2.II). The investigator's responses to this category must be brought before the full Committee for action at a regularly convened meeting.

C. **Conditional Approval - Additional Chair Review Required Before Implementation.** When the IRB's stipulations are minor in nature, (such as non-substantive issues that do not require judgment by the reviewer) the IRB may vote to authorize the Chair or another IRB member designated by the Chair, to review the investigator's responses under an expedited review procedure. If the responses are considered satisfactory, the continuation will then be approved for implementation by the Chair or designee.

D. **Disapproved.** This action indicates that the board identifies major ethical conflicts or safety issues in the project which cannot be remedied without major revision. Written notification from the IRB of the decision to disapprove a protocol is accompanied by reasons for the decision. As needed, the IRB assures the ongoing rights and welfare of enrolled subjects in consultation with the investigator or other health professionals involved in subjects' care. Disapprovals are reported to federal agencies when required, as described in SOP 17.1.

II. **Notifications**

A. Investigators are notified in writing through the electronic system of the decision of the IRB and any changes required.

B. Continued approval is not granted until all required changes have been made and submitted for review and approval. Once approved, the investigator is sent a letter that references the new approval period. In general, a re-certified consent form, indicating the new approval period, is accessible through the eIRB system. If the IRB Office has been informed that the study is closed to enrollment, a new consent form is not issued.

C. The KUMC Institutional Official (IO) is notified of committee action(s) through the meeting minutes. The KUMC Institutional Official (IO) has access to meeting minutes in a shared electronic folder and is notified of committee actions through communication with the HRPP Director.

6.7 **Study Expiration**

I. The expiration date of the project is the last day it can be conducted. When continuing review of a research protocol does not occur, or if approval conditions are not satisfied, prior to the end of the approval period specified by the IRB, approval expires automatically. The investigator will be informed by a system-generated notification from the eIRB system. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations.

II. Federal regulations make no provision for a grace period after study expiration. If project approval has expired, all protocol-related activity must cease, including, but not limited to, recruitment, enrollment, data analysis and study visits for ongoing subjects.

III. When informed of the expiration, the investigator should contact the IRB immediately if the expiration affects subject safety. Investigators may request continuation of protocol-related activity they deem necessary to ensure subject safety. If the investigator believes that some or all subjects may be harmed by study expiration, he/she must submit written documentation to the IRB chair, including a list of affected subjects. The IRB chair may determine that the specified activities may continue for affected subjects. At his/her discretion, the IRB chair may consult individual IRB members or the entire committee when making the determination. The IRB chair will provide written documentation to the investigator about the
study activities that may continue for affected subjects.

IV. When a lapsed project is submitted for continuing review, the investigator must submit a letter with the continuing review application summarizing any study related activities that occurred during the lapse.

V. If the principal investigator does not notify the IRB office within 30 days of expiration, the IRB office may administratively close the project in the IRB system.

6.8 Suspensions or Terminations for Cause

I. The IRB has the authority to suspend or terminate approval of human subjects research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected, serious, and related harm to subjects. Suspensions and terminations are discussed in IRB SOP17.1

II. Suspension is the temporary closing of some or all aspects of a human research project or discontinuing some or all of an investigator's privilege to conduct human subject research short of the permanent ending of all activities related to a human research project or an investigator's privilege of conducting human subjects research. Suspension may be for serious or continuing noncompliance with IRB policies or for threats to the rights and welfare of subjects. The suspension may be partial in that certain activities may continue while others may stop or it may be complete in that no activity related to the research may proceed. The IRB will make this determination. Termination is the permanent ending of all activities related to a human research project or an investigator's privilege of conducting human subject research at the University of Kansas Medical Center.

III. Decisions to suspend or terminate approved research are considered at a convened IRB meeting. When immediate action is required to ensure subject safety prior to a meeting of the convened IRB, research may be suspended or terminated by the IRB Chair. In the Chair's absence, the Institutional Official or HRPP Director can suspend the study on an urgent basis. Any notification of suspension or termination of approval includes a statement of the reasons for the IRB's action and is reported promptly to the investigator, the investigator's department chair, the Institutional Official. If the research is suspended outside of a convened meeting, the IRB is notified and reviews it at the next available meeting. The Institutional Official is responsible for further notifications outside the institution, in accordance with IRB SOP 17.1.

IV. In its notification of suspension or termination, the IRB will require, when applicable, immediate actions to notify subjects of the suspension or termination and any necessary steps to ensure the safety and welfare of subjects. Depending on the nature of the event and the subjects' best interests, they may be continued on an investigational drug, transferred to clinical care, placed under additional safety monitoring, or provided with other protective measures. If subjects are continued on the investigational drug or if they are followed up for safety monitoring after the suspension or termination, investigators remain responsible for notifying the IRB of any reportable adverse events or problems. Additional requirements may include remedial action or education for the investigator or any other key personnel.

V. When the IRB suspends a study, the IRB staff will change the status of the study in the electronic IRB system to "Suspended."

VI. Suspended research requires continuing review according to the previously-designated schedule, until such time as the research is terminated or closed or until the suspension is lifted. Terminated research does not required continuing review.

6.9 Sponsor-Imposed Suspensions

I. Notification of suspension by a sponsor unrelated to risk is submitted to the IRB for review and approval as a modification to previously approved research. Such modifications are considered minor and may be
reviewed by the expedited procedure.

II. When a sponsor or federal authority suspends the study for concerns related to safety or welfare of subjects, the suspension is reviewed by the convened IRB. The IRB considers immediate actions that should be taken for subject safety. As appropriate, the IRB also may consider future actions that would be necessary to allow resumption of the study. When the sponsor or federal authority suspends the study, this action will be reflected in the electronic IRB system by changing the study status to "Suspended" in order to inform the study team and the eIRB users of the current status.

6.10 Study Closure Procedures

I. Request for closure of a study is submitted by the investigator in the eIRB system. A study may be closed if

   A. The study is permanently closed to enrollment.
   B. All subjects have completed all study-related interventions.
   C. Collection of private identifiable information is complete.
   D. Analysis of private identifiable information is complete.

II. The investigator is notified in writing of the closure approval. IRB oversight is concluded at that time.

6.11 Activities related to Closed Studies

I. If the investigator wishes to re-contact former subjects after study closure, to provide additional study-related information, the communication must first be approved by the IRB.

   A. Requests to re-contact former subjects will be submitted as a Report of New Information the electronic IRB system and reviewed on an expedited basis by the IRB chair or other experienced member. At his/her discretion, the Chair or member may refer the request to the full committee.
   B. Communications that impact the safety of former subjects will be referred to a convened meeting. The Committee may request additional information to ensure that adequate follow-up occurs.

II. Investigators must obtain prior approval from the IRB if they wish to use identifiable data from their previously closed study for additional analyses. A new IRB application will be required.

III. Prior IRB approval is required if data from a closed study are used by persons not associated with the original study or if the data are to be used for purposes not covered by the original approval. This requirement applies for both identifiable and de-identified data. The IRB staff will evaluate the proposed secondary use, to determine whether the new activity is exempt or requires expedited or full-committee review and schedule an appropriate review.

   A. For identifiable data, investigators should submit a Retrospective Project Description
   B. If the data are de-identified, investigators should submit a request for a Determination of Not Human Subjects Research.

Approved By:
Vice Chancellor for Administration

Attachments:
Approval Signatures

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<td>Steffani Webb: Vice Chancellor for Administration</td>
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<td>Lisa Hoebelheinrich: Chief Compliance Officer</td>
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Applicability

KU Medical Center, KU SoM Wichita