1. PURPOSE
   1. This Standard Operating Procedure described the requirements for the process of Continuing Review of research conducted under the Carilion Clinic IRB
2. POLICY
   1. 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.
   2. When required, continuing review must be substantive and meaningful, and it must address any new information or changes that relate to risk/discomfort, benefits, safeguards for participants, and informed consent to assure that all criteria for approval specified under 45 CFR 46.111 and 21 CFR 56.111 are satisfied.
   3. When required, informed consent forms(s) will be reviewed to assess whether the information provided in the currently approved or proposed consent form is still accurate and complete, and whether any new information that may relate to the subject’s willingness to continue participation should be included in the document.
   4. For non-exempt research approved before January 21, 2019, continuing review will occur at intervals of no greater than 364 days until the closure of the study
   5. For greater than minimal risk research or research that is FDA-regulated and approved on or after January 21, 2019, continuing review will occur at intervals of no greater than 364 days until the closure of the study
   6. For research that meets one of the following categories and is approved on or after January 21, 2019, continuing review will not be required unless the rationale is documented by the IRB
      1. Is eligible for expedited review
      2. Is approved by limited IRB review:
      3. Data analysis, including analysis of identifiable private information or identifiable biospecimens and/or
      4. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care and not specifically for research purposes.
   7. The Carilion Clinic 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 Carilion Clinic IRB is the reviewing IRB; (3) associated with compliance concerns or (4) other factors determined and documented by the IRB.
   8. The IRB applies the same criteria for approval of continuing review as it does for initial applications.
3. RESPONSIBILITY
   1. The IRB committee, IRB Chair, IRB staff, or designee performs these procedures.
4. GENERAL PROCEDURE
   1. When complete continuing review materials are submitted to the IRB for review, a determination is made whether the continuing review is eligible for expedited review or if it should be scheduled for a convened meeting.
   2. If expedited review is not applicable, the Continuing Review will be placed on the agenda for review at the next available meeting.
   3. The Continuing Review application 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-Carilion sites, when applicable;
   4. All previously approved documents are housed within the electronic system and available at the time of the continuing review.
   5. If protocol amendments or other changes are required, the researcher must wait until the Continuing Review is approved.
   6. 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.
   7. When required by regulation or institutional policy, review of ongoing research must occur prior to the study <End Approval Date>.
      1. Approval and <End Approval Date> are calculated HRP-022 SOP: End Approval Dates
   8. 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)
   9. Reviewers (Primary reviewers in the case of Full Board Reviews) conduct an in-depth review of the provided materials. These reviewers should:
      1. 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;
      2. Consider issues regarding the investigator and the institution(s) where the research is being conducted during its continuing review, including:
         1. Changes in the investigator’s situation or qualifications (e.g., suspension of hospital privileges, change in medical license status, or increase in number of research studies conducted by the investigator);
         2. Evaluation, investigation, and resolution of any complaints related to the investigator’s conduct of the research;
         3. Changes in the acceptability of the research in terms of institutional commitments (e.g., personnel and financial resources, adequacy of facilities) and applicable regulations, State and local law, or standards of professional conduct or practice.
      3. Assess whether the information provided by the investigator at the time of continuing review is consistent with the research protocol previously approved by the IRB.
         1. Evaluate the number of subjects enrolled in the research at the time of continuing review to ascertain whether enrollment is consistent with the planned number of subjects described in the IRB-approved protocol.  A marked difference between the actual and expected rates of enrollment may indicate a problem with the research project that requires further evaluation, including whether the research project is likely to provide sufficient data to answer the scientific question(s) being posed.
         2. Review the number of subjects who discontinued their participation and a summary of the reasons for the withdrawals, if known. IRB review of this information may shed light on problems related to the conduct of the research.
            1. For example, a high rate of subject withdrawal secondary to serious adverse events may indicate that the risks of the research are greater than expected and may lead the IRB to conclude that the research should not be approved for continuation because the risks to subjects are not being minimized or are not reasonable in relation to the anticipated benefits to the subjects and the importance of the knowledge that may reasonably be expected to result.
      4. Consider if new or additional risks have been identified (e.g. unanticipated problems, DSMB reports) that would require changes to the protocol, consent form, review frequency, etc.;
      5. Consider if any new information may impact subjects' willingness to continue participation;
      6. Report to the IRB Chair or IRB staff if it appears that the research is not being conducted in accordance with IRB requirements;
      7. Determine the adequacy of the process for obtaining informed consent by reviewing a copy of the informed consent document submitted by the investigator to verify that the investigator is using the most recently approved version and that the document contains the most accurate, up-to-date information about the research.
      8. Confirm, in light of the above information, that the current consent is still accurate and complete;
      9. Determine, in light of the above review, whether or not the study continues to meet federal criteria for approval;
      10. Determine whether or not the continuing review interval should change.
   10. The IRB has the discretion to require external verification that no material changes have occurred since the previous review. External verification may be required:
       1. when the study is classified as high risk,
       2. when the investigator has previously failed to comply with IRB requirements,
       3. when materials submitted for continuing review include unapproved modifications or inconsistent information, or
       4. Studies for which the investigator’s conduct was questionable as detected at the time of continuing review or audit;
       5. when the IRB has been informed of non-compliance by another source.
       6. Complaints from research participants that appear not to be adequately addressed by the investigator;
       7. Studies for which the investigator also serves as sponsor;
       8. Studies with an unexpected frequency (high or low) or severity of reported serious adverse events;
       9. Studies with a high participant dropout rate;
       10. Studies where the IRB discovers previously undisclosed information regarding the investigator and/or a co-investigator after the IRB has approved the investigator and without an acceptable explanation by the investigator;
       11. Complicated studies involving an unusual level or types of risk to subjects;
       12. Studies requiring compliance with Carilion policies, including medication use, device use, and safe medication practices;
       13. Studies requiring auditing of medication use, storage and procedures;
       14. Other reasons determined by the IRB.
   11. Such external verification may include:
       1. A research Education Session by Carilion staff
       2. An audit performed by Carilion’s Organizational Integrity and Compliance Office (OIC)
       3. Observation of the consent process (per HRP-193 SOP Observation of the Consent Process)
       4. Review of communications between the FDA and the sponsor/IND holder
       5. Drug/device dispensing log
       6. NIH communications and reviews
       7. DSMB/DMC reports
       8. Back translation of consent form or other material to be used by research subjects
       9. Letters of review or approval from other collaborating IRBs or a Central IRB
       10. A site monitor report
       11. A sponsor/CRO audit
       12. Correspondence with the sponsor/CRO
       13. Other materials as determined appropriate
   12. If new issues arise during the course of the study that require additional expertise from outside the committee, any member may request that the HRPO Director or IRB staff arrange a consultant for the continuing review,
   13. The submission for all studies may include the following documents, as applicable:
       1. Continuing Review Form, which includes a summary of changes since the last review:
       2. Currently approved protocol
       3. Current informed consent document(s);
       4. For studies being monitored by a data monitoring committee or data and safety monitoring board, all safety monitoring reports for the reporting period;
       5. Any correspondence from the FDA;
       6. Device accountability log, for device studies;
       7. A copy of any FDA audits of sites under the auspices of the KUMC investigator;
       8. The most recent FDA progress report, for studies in which the KUMC investigator holds the IND or IDE
   14. The Committee may set approval periods and requirements for continuing review at intervals of less than one year but not greater than one year.
   15. If a study has been open for a period of three or more years and the PI has not enrolled subjects in the study or if enrollment in the study has been significantly below expectations for three years, the IRB may request the PI closes the study unless the PI can provide justification of extenuating circumstances and rationale for keeping the project open (e.g., the study is about a rarely seen condition).
   16. The <End Approval Date> of the project is the last day any research may be conducted. When continuing review of a research protocol does not occur, or if approval conditions are not satisfied, prior to the <End Approval Date> specified by the IRB, approval expires automatically.
       1. The investigator will be informed of the expiration by a system-generated notification from the PRISM system.
       2. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations
       3. 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
       4. When informed of the expiration, the investigator should contact the IRB immediately if the expiration affects subject safety.
          1. 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.
          2. 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.
       5. When a lapsed project is submitted for continuing review within 90 days of the lapse, the investigator must submit a letter with the continuing review application summarizing:
          1. Whether all research related activities stopped as of the expiration date or whether research activities continued after expiration
          2. If activities continued after expiration, include an explanation as to which specific research activities continued and the rationale
          3. An explanation of why the study expired without renewal
          4. A corrective action plan to prevent this from occurring in the future
       6. If the investigator does not submit a continuing review application within 90 days of expiration, the IRB office may administratively close the project and a new research application may be required to re-initiate the study. A continuing review application may not be accepted.
5. CONVENED BOARD CONTINUING REVIEW
   1. Review is conducted by the convened board as required by the Revised Common Rule, by FDA regulations or as deemed necessary by the IRB.
   2. Continuing review materials referenced above and as applicable to the study are available to all IRB members within PRISM, along with all other review assignments, at least 5 days prior to the meeting.
   3. One member is assigned as the primary reviewer for the continuing review.
   4. 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.
   5. 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.
   6. After discussion, the IRB determines whether the study continues to meet federal approval criteria and votes on one of the actions listed in HRP-106 SOP - Committee Review Conduct.
6. Expedited Continuing Review
   1. Continuing review for HHS-regulated research that is greater than minimal risk may be provided on an expedited basis if no subjects have been enrolled to date and no additional risks have been identified.
   2. 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 above. Continuing review of FDA-regulated research may occur by expedited procedures when the research is:
      1. 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
      2. Where no subjects have been enrolled and no additional risks have been identified; or
      3. Where the remaining research activities are limited to data analysis.
      4. Where the study involves a humanitarian use device
   3. 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.
   4. 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.
      1. 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.
   5. The IRB Chair or a qualified member(s) reviews the request for continuation to ensure compliance with current regulations and standards.
   6. The designated reviewer documents the review in the electronic IRB system.
   7. 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 PRISM system.
7. APPROVAL AND REVISIONS
   1. 07 APR 21: HRPO Director, Carley Emerson, originally created and approved
8. REFERENCES
   1. None