Series 409 Continuation Reviews, Renewals and Approvals

Continuation Reviews, Renewals, and Post Approval Monitoring from Series 409 of the Standard Operating Procedures

January 21, 2019 marked the effective date of substantial revisions to the Common Rule. One of those revisions, designed to decrease administrative burden and increase meaningful oversight, is the elimination of the continuation review requirement for most studies. Studies that are greater than minimal risk or otherwise reviewed by the Convened IRB still require annual Continuation Review.

For all other studies, the annual Continuation Review requirement has been replaced with the following regulatory mandates by the IRB (45 CFR 46.108): (a) determine which projects require review more often than annually; (b) determine which projects need verification from sources other than the investigators that no material changes have occurred since the last IRB review; (c) Ensure the prompt reporting of proposed changes; (d) Implement systems that ensure that investigators will conduct the research activities in accordance with the IRB approval on file; and (e) Establish procedures for ensuring prompt reporting to the IRB and others of reportable events.

Protocols that received approval prior to January 21, 2019 remain subject to the annual Continuation Review process outlined in Section VII, below. Other protocols will be subject to Post Approval Monitoring (PAM).

I. Annual Administrative Check In (PAM)

All studies that are not subject to one of the items below will receive an annual administrative check in via email (including exempt studies). No investigator action is required for an Administrative Check In; instead, it is designed to be more of a re-training about the requirements of keeping a protocol up-to-date and in line with ethical and policy requirements for the protection of human participants in research.

During the initial review process, IRB member reviewers will be directed to select the level of Post Approval Monitoring that they think is most appropriate for the protocol under review. Continuation review more frequently than the five year time frame established by SOP 405 is one of the options, and the IRB member reviewer will document a reason for requesting that review, when applicable.

II. Site Visit & Assessment (PAM)

The Site Visit & Assessment is a training tool designed to be engaged with by HRPP staff and the research team together. Five percent of all Active Expedited studies with an initial approval date in that month will receive a Site Visit & Assessment, regardless of the selection made by the reviewer at the time of initial review. Entry into the pool of studies will be randomized using a random number generator. Studies for which the PI has had another Site Visit & Assessment successfully completed within the last six months will be removed from the pool of studies. The results of the Site Visit & Assessment will be made available to the IRB/HREC in the monthly report.

When a study is selected for a Site Visit & Assessment, the research team will be provided with the list of items HRP staff will be coming to assess in advance of the visit. The visit will be scheduled for a mutually agreed-upon time, but must be completed prior to the end of the month in which approval for that study was granted barring extenuating circumstances. The Site Visit & Assessment will examine the following:

- The Informed Consent process, if ongoing

- Records related to recruitment
- Informed Consent documentation, if applicable
- Data/Specimen storage locations & security
- Staffing
- Participant feedback, concerns, complaints

The research team will receive findings and, if applicable, corrective instructions following the visit. It is anticipated that corrective instructions will largely take the form of a Deviation, when it is present at all.

Twenty percent of all Active protocols that gained approval in that month will receive a combination of the following types of Post Approval Monitoring, according to the selection made by the reviewers at the time of initial review. In sum: 25% of all Active protocols with approval dates in that month will receive some level of Post Approval Monitoring activity that requires some effort by the PI; 75% will receive the Annual Administrative Check In.

III. Self-Assessment (PAM)

The Self-Assessment is a training and education tool that makes the Site Visit & Assessment materials available to the Principal Investigator, and requests that they complete the checklist themselves, which is also due at the end of the month in which initial approval was levied.

IV. Informed Consent Process Review (PAM)

The Informed Consent Process review entails having one member of the research team or the HRP staff observe the Informed Consent process with at least one participant. The second member of the research team or the HRP staff member will complete a short checklist that is designed to ensure that the Informed Consent process is taking place as stated in the protocol. Checklists will include the following topics:

- Was the most current version of the informed consent document used?
- Did the process occur in the setting contemplated in the protocol?
- Was the participant given an opportunity to ask questions?
  - Were those questions answered?
- Did the participant exhibit understanding of the research procedures? If not, are there modifications the research team might make to the process to enhance understanding?
- Was a copy of the informed consent document given to the participant?

V. Informed Consent Document Review (PAM)

The Informed Consent Document review entails making the documentation related to the informed consent process available to HRP staff for verification that it is being properly documented, stored, and accessed. Items checked in this review include:

- Ensuring that all optional selections are being attended to,
- Checking to be sure that signatures and dates are being obtained, where appropriate;
- Ensuring that children are not signing for both children and parents, on Permission & Assent forms; and
- Verifying that documents are being stored according to the procedures outlined in the protocol.

VI. Study Team Review (PAM)

The Study Team review requests that the Principal Investigator review the Active Study Staff listed on the protocol, and verify:

1. That the list is correct or that an amendment will be filed within five business days
2. That all CITI trainings are active for all study personnel; and
3. That no Conflicts of Interest exist with any member of the study team.

VII. Annual Continuation Review

Protocols that received approval prior to January 21, 2019, must continue to go through annual Continuation Review procedures to obtain renewal. In addition, protocols approved on or after January 21, 2019, which have been Approved for 5 years will obtain Continuation Review before obtaining a sixth year of eligibility; this structure shall remain in place for renewal every five years until the protocol is closed.

Investigators will be prompted to submit a Status Report no more than 30 days prior to the expiration of their protocols. It is the research team's responsibility to submit a Status Report on time, to permit sufficient time for IRB review of the project. The Status Report Form shall include, at a minimum, the following information:

- The number of participants accrued;
- A summary since the last Convened IRB review of:
  - Adverse events and adverse outcomes experienced by research participants;
  - Unanticipated problems involving risks to participants or others;
  - Participant withdrawals and the reasons therefor;
  - Any complaints about the research;
  - Any unreported modifications;
  - Any relevant recent literature produced as a result of the research project; and
  - Any interim findings.
- Any relevant reports from other research sites
- The researcher's current risk vs. potential benefit assessment based on analyses conducted to date

The IRB will use the Expedited Review Process outlined in SOP 405 to determine that the criteria for approval remain intact, and that no updates provided in the Status Report require modification or constitute reportable events. When continuing review of research is required by law or regulation, IRB members will determine whether the protocol needs verification from sources other than the researchers that no material changes have occurred since the last review by the Convened IRB. Members of the IRB use the information to determine whether the study may continue, whether the current informed consent document is complete and accurate, whether any significant new findings have arisen that might relate to participants' willingness to continue participation, whether additional information about the study should be provided to participants, whether changes to the research will be required, and whether any reason exists for the study to be suspended or terminated. Upon approval of the protocol, a new expiration date will be assigned. For protocols gaining initial approval prior to January 21, 2019, the new approval period shall be no more than 364 days. For protocols gaining initial approval on or after January 21, 2019, the period of approval shall be five years from the expiration date, or the date on which the research team indicated all study procedures would be complete; whichever occurs first.

For protocols that received initial approval by the Convened IRB, it is critically important to submit the Status Report as soon as a reminder of expiration is received. The Convened IRB completes continuation reviews at its regularly scheduled meetings, and materials must be distributed to the IRB at least five days in advance of the meeting prior to the protocol's expiration. Failure to timely submit a Status Report will result in protocol expiration.

VIII. Convened IRB Review & Expedited Continuation Review

Protocols that received their initial approvals via the Convened IRB Review process may become eligible for Expedited Review processes under guidance developed and released by the Office for Human Research Protections. Eligibility for Expedited Review may occur under the following circumstances:

1. Where
   a. The research is permanently closed to the enrollment of new subjects
   b. All subjects have completed all research-related interventions; and
   c. The research remains active only for long-term follow-up of subjects; or where no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis.

2. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.