SOP 404: Continuing Review & Study Closure

Terms and Abbreviations

FDA: Food and Drug Administration

IO: Institutional Official – individual who is legally authorized to act for the institution and ensures the effective functioning of the IRB

IRB: Institutional Review Board

IRB office staff: the IRB Manager, IRB Administrator, and any other IRB office staff, either collectively or individually

PI: Principal Investigator

UWM: University of Wisconsin – Milwaukee

Overview

The initial approval of research is based on both the PI's presentation of information and the IRB's assessment of the risks, benefits, and anticipated results of the research as set forth in the protocol application. At the time of initial review, the IRB determines a period of approval and the frequency of any continuing review based on the type and degree of anticipated risk for subjects and/or others.

Depending on the degree of risk, the IRB may conduct continuing review at a fully convened meeting, may conduct continuing review under expedited review procedures, or may not require continuing review. If continuing review is not required, the PI will need to report whether the study is active or closed on a routine basis (every year for studies eligible for expedited review and every three years for studies that qualify for an exemption).

The IRB may approve the research for a period less than one year when deemed necessary. Examples of studies that might receive a shorter review period would be if there are concerns regarding the risks of the study, the PI's level of experience or competency to conduct the research, or a history of non-compliance with IRB-approved protocols or institutional policies and procedures.

If the IRB believes or finds that an investigator has not conducted the research according to the IRB-approved protocol, the IRB may require verification from sources other than the investigator that no material changes in the conduct of the research have occurred since previous IRB review and approval (e.g., auditing or monitoring of consent documentation). This verification should be in writing and submitted for IRB review along with the Continuing Review Form. Any requirement of verification will be communicated to the PI by the IRB in writing.

The IRB conducts continuing review of research covered by this policy at intervals appropriate to the degree of risk. This means that continuing review will occur on or before the end of the approval period.

If continuing review is not required, the IRB will still require periodic updates, in writing, regarding the study status from the PI. If the PI does not submit a study status update prior to the established date, the IRB will close the study.

Details and Procedures

Required Content for a Continuing Review:

1. The most current IRB approved protocol, informed consent document, and recruitment material.
2. A continuing review form that includes:
    a. A summary of the progress of the research at UWM and other sites, if appropriate.
    b. A summary of any preliminary results or findings from this research at UWM and other sites.
    c. A summary of any recent literature, findings, or other relevant information that might affect the risks associated with the research, the risk-benefit analysis, or a subject's willingness to continue participation.
    d. The total number of subjects accrued since the initial approval or the last continuing review and the total number of subjects enrolled to date.
    e. A summary of recruitment and informed consent process information and mention of any problems.
    f. A summary of any unanticipated Adverse Events that have occurred since the initial review or the most recent continuing review, including whether they were of unanticipated frequency and/or severity, related to the research intervention itself, procedure, drug, device or biologic, and whether they modify the risk-benefit analysis, result in modifications to the research protocol to further minimize risk, and/or to the informed consent document.
    g. A description of any amendments to the research protocol or informed consent documents that have been reviewed and approved by the IRB since the most recent initial or continuing review approval.
    h. Any proposed amendments to the research protocol or informed consent documents

Continuing Review Determinations

1. The IRB makes the following determinations to approve research for continuation:
    a. That the research continues to satisfy the criteria set forth in 45 CFR § 46.111 regarding minimizing risks, the anticipated risks remain reasonable in light of the potential for benefit, and there is a plan for an equitable selection of subjects, an adequate informed consent process and documents, provisions for monitoring the data for safety, and provisions to ensure the privacy of subjects and confidentiality of data collected.

b. Where applicable, the additional protections for vulnerable subjects such as pregnant women, fetuses, prisoners, and children as specified by regulations and the IRB, are in place and remain adequate.
c. That the informed consent documents are accurate and complete, and any significant new findings that may affect a subject's willingness to continue participation have been incorporated into the documents and communicated to research subjects in active treatment, if the IRB determines such information might affect their willingness to continue in the research.
d. Whether the research requires verification from sources other than the PI (e.g., other institutional review boards, the FDA, Sponsors, or institutional sources or committees) that no material changes in the research have occurred since the previous review. The IRB may request an audit of study files to ensure adequate protections if there are concerns that there may have been material changes without prospective IRB review and approval.

Continuing Review by the Convened IRB

1. An online continuing review form must be submitted on or before the IRB meeting submission deadline for full committee review.
2. For research that was initially approved by the full board IRB as more than minimal risk, continuing review will also be conducted by the full board IRB using the same procedures used during initial review.
3. The IRB may make the following decisions:
    a. Approved: Approve as submitted.
    b. Approved with Conditions: Conditional fulfillment is required to secure approval. The PI's response may be reviewed through expedited procedures.
    c. Tabled: Table the discussion of the research because additional information and/or protocol revisions are required.
    d. Disapproved: The research protocol cannot be approved as proposed.
4. The decisions will be based on the votes of a simple majority (more than 50%) of the voting members present at a full board IRB meeting.
5. The IRB office staff communicates the determinations of the IRB, in writing via email, to the PI and co-investigators, if applicable.
6. Meeting minutes are sent to the IO monthly and made available to others within the institution upon request, so all can be aware of the IRB actions.

Review by Expedited Procedures

1. For research protocols the IRB initially approved under expedited procedures or determined by the full board IRB to be minimal risk, the IRB conducts continuing review under expedited procedures. If new risks or information have been identified by the PI or IRB reviewer, full board review could be warranted.
2. Research protocols previously approved by the full IRB may be eligible for review under expedited review procedures in accordance with 45 CFR § 46.110, under either Category 8 or 9:
    a. **Category 8**: Continuing review of research previously approved by the full board IRB as follows:

i. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow up of subjects; or
ii. Where no subjects have been enrolled and no additional risks have been identified; or
iii. Where the remaining research activities are limited to data analysis.

b. **Category 9**: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Categories 2 through 8 do not apply but the IRB has determined and documented at a full board meeting that the research involves no greater than minimal risk and no additional risks have been identified.

3. The IRB is informed of all continuing reviews approved under expedited review procedures on the next available meeting agenda and this is documented in the IRB meeting minutes in accordance with 45 CFR § 46.110(c) and 21 CFR § 56.110(c). Meeting minutes are sent to the IO monthly and made available to others within the institution upon request.

Study Status Update (continuing review not required)

1. The following IRB approved protocols do not require continuing reviews.
   a. Studies that qualify as exempt research under 45 CFR 46.104
   b. Studies approved after January 21, 2019 under expedited review procedures (unless the study must also comply with FDA regulations or the IRB determines and justifies that continuing review is required and communicates this to the PI)
   c. Studies approved after January 21, 2019 by the convened/full IRB and have progressed to the following activities:
      i. The study is not required to apply FDA human subjects research regulations, and
      ii. Data analysis, including identifiable private information or identifiable biospecimens, or
      iii. Accessing follow-up clinical data from procedures that subjects would undergo as part of their clinical care.
2. The UWM IRB will require study status updates as described below.
   a. Exempt Research
      i. Expiration dates will be three years after initial approval and three years after each notification to the IRB that the study is still active.
      ii. The PI must report the current study status, i.e. whether the study is still active or can be closed.
      iii. If no study status is submitted to the IRB by the expiration date, the IRB will close the study and the PI will receive an email notification of the close out.
   b. Expedited Review Research or Research approved by a convened IRB that is in data analysis or follow-up clinical data stages. Research must have an initial approval date on or after January 21, 2019.
      i. Expiration dates will be one year after initial approval and one year after each notification to the IRB that the study is still active.
      ii. The PI must provide the following information to the IRB
         1. Status, i.e. whether the study is still active or can be closed.

2. Any changes to funding status.
3. Whether there have been any changes to the approved study materials, and the date of IRB amendment approval.
4. Any changes to the study risks or whether any protocol deviations, problems or unexpected events related to the study have occurred.

iii. If no study status is submitted to the IRB by the expiration date, the IRB will close the study and the PI will receive an email notification of the close out.

Expiration Dates

After the initial approval period, the IRB may use one of two methods for determining the expiration date for subsequent continuing reviews:

1. The expiration date is calculated based on the date that the IRB office staff determine any conditions are met and issue the continuing review approval letter.
   Example: A study is initially approved for 12 months on May 2, 2019 and expires May 1, 2020. IRB office staff issue the approval letter on April 30, 2020. The new expiration date will be April 29, 2021.
2. If a review is completed within 30 days of the expiration date, the original expiration date may be retained and carried from year to year.
   Example: A study is initially approved for 12 months on May 1, 2020 by the full board. The study expires April 30, 2021, but the closest full board review date is April 2, 2021. If the board approves the continuing review on April 2, 2021, IRB office staff may elect to retain the April 30 expiration date. The new approval period would be May 1, 2021 – April 30, 2022.

Study Completions and Close Outs

1. IRB approved studies may be closed in the following circumstances:
   a. All study activities, including data analysis, are complete
   b. Study activities are limited to the analysis of de-identified data and/or report writing. There is no possible way for anyone to link data to individual subjects and any key linking study IDs to subject identifiers has also been destroyed.
2. Studies requiring Continuing Reviews.
   a. If a study meets the criteria for closure listed above, the PI must complete and submit the Continuing Review Form to the IRB.
   b. Once submitted, the IRB will acknowledge the completion/closing of the study and terminate IRB approval.
   c. If a continuing Review Form is not received by the IRB prior to the study expiration date, the study will be closed by the IRB and a close out notification will be sent, via email, to the PI.
3. Studies not requiring continuing reviews
   a. If the PI notifies the IRB that the study is complete, the IRB office staff will maintain a record of the update in the study file and terminate IRB approval.
   b. If no study status is submitted to the IRB by the expiration date, the IRB will terminate the study and the PI will receive an email notification of the close out.

References

45 CFR § 46 (Common Rule)

21 CFR § 56 (FDA)

OHRP Continuing Review Guidance (2010)

Revision History

Version	Date	Summary of Changes
1	2 Jul 2020	Initial version