



Campus Institutional Review Board
University of Missouri-Columbia

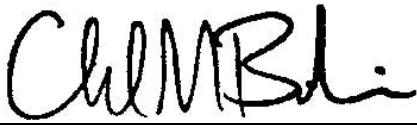
Continuing Review Process

Policy Number 2876.29

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Effective Date: December 12, 2007

Board Review

Signed 
IRB Chair

Date December 12, 2007

Administrative Review

Signed 
Associate Vice-Chancellor for Research

Date December 12, 2007

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1.0 Policy

The Campus Institutional Review Board (Campus IRB) assures that all human subject research conducted under its jurisdiction is afforded the opportunity for renewal in the form of a continuation review process. The Campus IRB will apply the guiding principles of the Belmont report when monitoring the research mechanisms that are in place to constantly protect the safety and welfare of subject participants.

2.0. Scope

The continuing review process applies to all human subject research being conducted under the jurisdiction of the University of Missouri-Columbia that requires review and approval of the Campus IRB.

3.0 Purpose

The Campus IRB must assure that the Continuing Review Process has the same protections offered in the initial review and approval processes, by assessing that the ethical principles and safeguards for research are appropriately applied in a dynamic ongoing manner.

4.0 Standard Operating Procedure

The Campus IRB shall have authority to grant continuing approval for projects involving human subject research. The Campus IRB shall also have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head. Any suspension or termination of approval shall comply with the "Suspension and Termination" Policy.

The Campus IRB will determine the approval interval and delineate the expiration date by which investigator(s) must submit a Continuing Review Report (CRR).

The review period shall be set for any length, but shall not exceed 12 months from the date of the initial approval date or continued approval date.

I. CAMPUS IRB CRR REVIEW PROCESS

BACKGROUND: Federal regulations require the CRR process to be substantive and meaningful. When considering whether or not to renew a study, the CIRB will review the CRR report, all supportive documents, and the investigator responses and revisit the same criteria used to grant initial approval and must determine that:

- a. The risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
- b. The selection of subjects continues to be reasonable in relation to anticipated benefits;
- c. Informed consent continues to be appropriately obtained and documented;
- d. There are appropriate provisions for safety monitoring of the data, if necessary;
- e. There are protections in place ensuring the privacy of the research subjects and confidentiality of the data.

- f. Appropriate safeguards have been made for vulnerable populations.

A. CRR SUBMISSION PROCESS

The IRB must conduct continuing review of human subject research projects for purposes of renewal of the IRB approval period, at intervals appropriate to the degree of risk, which is determined at the initial review, but *not less than once per year*. "Not less than once per year" means that the research must be reviewed on or before the one-year anniversary date of the previous IRB approval date, even though the research activity may not have begun until some time after the IRB gave its approval.

The Investigator shall submit their continuing review report in the amount of time sufficient to assure that it can be timely reviewed by the Campus IRB. The investigator shall **SUBMIT** a complete report by the deadline prior to the expiration of the study, to assure a timely review may be possible by the expiration date specified by the Campus IRB.

All CRR must be complete and properly submitted and received by the CIRB at least 45 days prior to expiration of IRB approval. Properly submitting the CRR at least 45 days prior to expiration of IRB approval will help to avoid delays in review or expiration of IRB review or approval. The investigator should contact the IRB if they have questions about the process or deadlines.

The Campus IRB is charged with conducting all continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

What activities will require you to submit a CRR?

1. Any previously approved human subject research project that has not been closed, completed or withdrawn through CIRB procedures.
2. If the research remains active for long-term follow-up of participant and data analysis that involves collection or analysis of identifiable information.
3. Data Analysis where the remaining research activities are limited to the analysis of data that at the time of collection includes identifiable private information as defined in 45 CFR 46.102(f)(2).
4. Active Data Collection on previously approved research.

When do you submit the CRR?

The investigator must properly electronically submit a CRR at least 45 days prior to expiration of IRB approval. The investigator must timely submit a complete CRR properly to avoid delays in the review process or expiration of IRB approval.

How do you avoid expiration of IRB approval?

The Investigator is required to assure the Continuing Review Report is complete and properly submitted and received at least 45 days to permit enough time for proper IRB review. If the report must be reviewed by a convened board, failure to submit the report by the 45 day deadline could result in expiration of IRB approval if the file is not complete in time to be placed on the board meeting docket. The investigator should make every effort to submit a complete report. An incomplete report may result in delays in the review process and could result in expiration of IRB approval if the board doesn't have enough information to approve the project.

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Expiration of Approval Period

The “expiration date” is the last date on which the research may be conducted and will be determined by the IRB at the initial and continuing review intervals. The “expiration Date” is a specific date determined by the Campus IRB which represents the end of the current Campus IRB approval period. The Campus IRB does not offer a grace period extending the conduct of human research beyond the expiration date of IRB approval. Requests for extensions beyond the expiration date will not be granted for any reason.

Projects may be approved for no longer than one year in any instance, but under certain circumstances may be granted a shorter approval interval. Enrollment of new participants may not occur after the expiration of Campus IRB approval. Continuing review and additional review approvals of research must occur on or before the date when Campus IRB approval expires.

Research interventions or interactions involving already enrolled participants should only continue with written documentation that the Campus IRB finds that it is in the best interest of the individual participants to do so and when the Campus IRB has confirmed that the PI is actively pursuing IRB renewal. The Campus IRB has the authority to make this determination, not the investigator. All Continuing Review Processes must comply with the “CIRB Review Process” policy.

If a Continuing Review form is not received by the deadline as required in the CRR renewal notice, and the report is not reviewed and approved before the expiration date, the IRB approval automatically expires and the investigator will be required to submit a new application for approval before being permitted to continue to conduct those research activities. Such expirations of CIRB approval will not be reported to OHRP as a suspension of CIRB approval under HHS regulations.

Expirations of IRB approval do not qualify for Priority Review Status. Federal regulations do not permit an incomplete or Continuing Review Report in which the approval has expired, to be approved beyond the expiration date.

The Campus IRB will not review Continuing Review Reports submitted after the IRB approval expiration date. Continuing to conduct human subject research activities after IRB approval expires is a Compliance Breach subject to action by the Campus IRB. See “Noncompliance Procedures” Policy. No human subject research activities should be conducted after the IRB approval has expired.

B. HOW IS THE CONTINUING REVIEW INTERVAL DETERMINED?

HHS regulations at 45 CFR 46.108(b) and 109(e) require, respectively, that an IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less frequently than once per year. The Campus IRB will conduct its continuing review processes in compliance with the “CIRB Review Process” policy. See policy.

At the time of the initial and continuing review, the CIRB will make a determination regarding the frequency of review intervals of the research protocol. All protocols will be reviewed at intervals appropriate to the degree of risk, but no less than once per year for the duration of the research (including when study activity is limited to long-term follow-up and data analysis that involves collection or analysis of identifiable data), reflected appropriately in the minutes and in compliance with the “Minutes” and “Assessing the Level of Risk” policies.

Research involving children as participants shall be determined in accordance with the requirements of 45 CFR 46.404-406 and Campus IRB policies governing child research subjects. (See “Recruitment Processes” and “Recruiting Vulnerable Subjects”).

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Research involving adult populations will be classified according to the level of risk in compliance with 45 CFR 46.102(i) and in accordance with the “Assessing the Level of Risk” policy.

In some instances, a shorter review interval may be required based on considerations of the potential or actual risks of the research, the degree of research intervention, the number of participants enrolled, any specific vulnerabilities associated with the research population, and /or the magnitude or frequency of risk to participants. The CIRB committee’s action taken and review interval will be reflected in the Minutes in accordance with the “Minutes” policy. If the review interval assigned is less than one year, the review period will begin the date the protocol is approved for participant accrual so long as the approval period does not exceed one year.

C. THE INVESTIGATOR RESPONSIBILITIES: CRR Submission Requirements

The investigator must submit the following on the CRR report for review by the Campus IRB in compliance with the CIRB Review Process Policy. (See Policy):

1. Any modifications in the Selection Process
2. Any modifications in the Recruitment Process
3. Assure that the Informed Consent Document is active and current if actively collecting data
 - i. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document.
4. Number of participants accrued to date
5. Report of Significant Findings that arose during the completion of the CRR report
6. Participant Benefits and potential risks subjects
7. Amendments or modifications
8. When studies were completed prematurely and why.
9. Number of unanticipated problems to participants or others; and a detailed explanation of the process implemented to address the problem.
10. Number of adverse events to participants or others; and a detailed explanation of the process implemented to address the event.
11. Number of compliance breach activities; and a detailed explanation of the process implemented to address the activities.
12. Number of subjects making Complaints; reason for the complaints; and a detailed explanation in support of the action taken.
13. Number of subjects who withdrew from the study; an explanation why they withdrew; and a detailed explanation in support of the action taken.
14. Number of Previous IRB Approval Suspensions of the research due to compliance, record-keeping or other concerns
15. Number of Previous IRB Approval Terminations of the research due to compliance, record-keeping or other concerns
16. An explanation of whether you intend to do Long-Term follow-up with a participant (even if enrollment is closed, all research related interventions have completed, or when activities were limited to collect of private identifiable information).
17. Any relevant recent literature related to the outcome of your research activities
18. Any interim findings
19. A current risk-benefit assessment based on study results.
20. New Conflict of Interest Disclosures (Attach the COI Committee Decision if applicable).
21. Justification for the continued use of a previous waiver of informed consent procedures.

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The Campus IRB recognizes the logistical advantages of keeping the approval period constant from year to year throughout the life of each project. Investigators proposing to conduct research beyond the original expiration date must comply with the “Continuing Review Process” Policy. See Policy. Additionally, all CRRs will be reviewed in compliance with the “Complaints” and “Unanticipated Problems and Adverse Events” policies.

When continuing review occurs annually and the Campus IRB performs continuing review within 30 days before the IRB approval period expires, the Campus IRB may retain the anniversary date as the date by which the continuing review must occur.

Investigators who submit continuing reviews with no intent to enroll additional participants do not need to submit a copy of the informed consent document for Campus IRB re-approval and stamping. However, the research study cannot be re-opened to enrollment without an amendment including a current informed consent document. The Campus IRB determines the appropriate review interval based on the federal regulations and University of Missouri Human Research Protections Program procedures. For continuing reviews that occur after initial approval, the Campus IRB verifies that the currently approved and correctly date-stamped informed consent documents have been submitted for review.

NOTE: Closure of activities will require submission of a Human Subject Research Activities Completion/Withdrawal Report.

D. CAMPUS IRB REVIEW OF THE CRR

All CRR applications will be reviewed in accordance with the CIRB Review Process Policy, whereby the application and investigator responses undergo the same review procedures as the “initial review process.” The CRR is compared to the original application and any amendments, modifications, deviations, adverse events, unanticipated problems, compliance breaches, or submissions subsequent to the initial review process. CRR applications submitted to the convened IRB are reviewed in compliance with the “CIRB Review Process” policy, but must be submitted by the deadline to be reviewed at the scheduled convened IRB meeting. See Policy. The IRB will review any applicable reports, which may include but not limited to local, on-site unanticipated problems involving risks to subjects or others, interim results and any other information needed to ensure that will facilitate a substantive and meaningful review.

MEMBERSHIP REVIEW RESPONSIBILITIES

All members are provided and expected to review:

- The Initial IRB Application form
- The Continuing Review IRB Application form
- The current consent document
- Any newly proposed consent documents
- All primary reviewers are provided and expected to review in depth:

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- The Initial IRB Application form
- The Continuing Review IRB Application form
- The current consent document
- Any newly proposed consent documents
- The complete protocol including any protocol modifications previously approved by the IRB.

E. THE CRR PROCESS AND DATA SAFETY MONITORING BOARD

The CIRB shall be kept apprised of any research activities requiring oversight by a DSMB (whose responsibilities include review of adverse events, interim findings and relevant literature) and may request the investigator provide a report from the DSMB. The board may also request the investigator provide additional information applicable to the research activities, interim findings and any recent literature that may be relevant to the research.

F. CRITERIA TO DETERMINE WHICH RESEARCH STUDIES REQUIRE REVIEW MORE OFTEN THAN ANNUALLY

The Campus IRB may request a shorter or altered Continuing Review interval, at its discretion, to further protect human subject participants. The Campus IRB may shorten the continuing review interval for any of the following, but not limited to:

1. Review changes may occur because of information provided in the initial application, amendment, deviation, breach report suggesting an increase risk to subjects;
2. Increased risk to subjects;
3. Any significant new findings that arose during the research process and may relate to a participant's willingness to continue participation;
4. Unanticipated events, problems or adverse event;
5. Complaints
6. Vulnerable subject populations;
7. Concerns regarding the research ethics of the Principal Investigator or team members;
8. Inadequate research team member training;
9. Conflict of interest;
10. Concerns regarding adequate resources to conduct research;
11. Any Compliance Breach
12. Any learned information that the Campus IRB deems relevant and necessary to assure the safety and welfare of human subjects.

G. FAILURE TO SUBMIT THE CRR

Failure to submit a CRR or to inadequately complete the report prior to the expiration date will result in immediate expiration of IRB approval by the Campus IRB. Investigator(s) will be notified that the project has expired.

If the CRR approval expires, the investigator is prohibited from conducting human subject research activities. The investigator must contact the Campus IRB for directives to either:

1. Complete a new application
2. Complete an Expired Approval Project Status Report

If the CRR approval expires and the investigator continues to conduct human subject research, the activities are proscribed by the CIRB. Conducting research without prior IRB approval is a Compliance Breach which is a very serious matter. The investigator must contact the Campus IRB for directives to either:

1. Complete a new application; OR
2. Complete a Compliance Breach Report AND a new application; OR
3. Complete an Expired Approval Project Status Report

H. ACTIONS TAKEN BY THE CAMPUS IRB ON CONTINUING REVIEW REPORTS (CRR)

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The Campus IRB may take the following actions on Continuing Review Reports in compliance with the “Campus IRB Review Process” policy. See policy.

If the IRB disapproves a proposed research activity, written notification must be provided to the investigator with a statement of the reasons for its decision, with the opportunity for the investigator to respond in accordance with the “Campus IRB Review Process” policy.

A copy of all approved IRB Minutes are provided to institutional officials in accordance with the “Reporting” policy to meet the requirements for notification to the organization of IRB findings/actions.

I. CRR APPROVAL NOTICE TO INVESTIGATOR

“The investigator(s) will receive written notice of the Board’s findings and decision on the proposal in a timely manner. The IRB will notify investigators in writing of all decisions to approve research activities, disapprove research activities, or require modifications to secure IRB approval of research activities. The Staff will assure the investigator receives written notification of the terms, approval and expiration date determination .”

Investigators will be informed in the “Approval Letter” of the scheduled continuing review interval of the project. Continuing review is mandatory for all active research projects including those that have been closed to subject accrual but are still involved in the data collection or analysis. Continuing review is also mandatory for research projects wherein an investigator is requesting withdrawal or closure.

Investigators will receive additional notice of the scheduled continuing review approximately 90 to 60 days prior to the expiration of the approval period. A CRR must be submitted online, at the earliest opportunity, to avoid interruption with IRB approval – at the latest 45 days prior to the current approval expiration in order to be reviewed, presented and acted upon by the Campus IRB before approval expires. It is the responsibility of the investigator to assure that all requests for documentation and information are submitted to the Campus IRB in a timely matter.

J. CRR EXPIRATION NOTICE TO INVESTIGATOR

Investigators submitting untimely CRRs risk automatic expiration of IRB approval if the report is not reviewed prior to the expiration of IRB approval. The Campus IRB will notify the investigator(s) via a written notice of the Board’s findings and decision regarding the CRR Expiration Notice. The IRB will notify investigators in writing of all decisions to expire or disapprove research activities. The Staff will assure the investigator receives written notification of the rationale for the decision and expiration date determination. The investigator(s) should contact the Campus IRB regarding any plans to continue research activities involved in a project with an expired CRR or approval status. The Campus IRB will conduct its activities in accordance with the “Reporting” and “Record Keeping” policies. Researchers who continue to conduct human research activities in the absence of IRB approval are deemed “noncompliant” and must comply with the “Noncompliance Procedures” policy. If applicable, the investigator should contact the Campus IRB immediately.

The Investigator must submit an “Expired Approval Project Status Report” if proposing to continue the research activities on the expired or terminated project, and a new application must be submitted. All research must cease (unless directed otherwise by the CIRB) until IRB approval has been obtained. The Campus IRB will required list of participants for whom stopping research activities would cause harm.

K. DOCUMENTATION

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The Campus IRB must document all review actions, including but not limited to the initial and continuing review, and note the frequency for the next continuing review in accordance with the "Record Keeping" policy. All review and approval periods are automatically date stamped after data is entered into the eIRB system by the Campus IRB. The continuing review interval may be shortened if the Campus IRB deems necessary. All Approval and Expiration dates, and Continuing Review intervals require documentation in the record. Intervals shorter than a one-year (12 month) period require specific documentation in the record.

Revised December 2006
Revised June 2007
Revised December 2007
Revised February 2008