

Study Closure, Lapse in IRB Approval and Withdrawal of Research

310 AOB (MC 672)
1737 West Polk Street
Chicago, IL 60612-7227
Phone: 312 996-4995 Fax: 312 413-0238
www.research.uic.edu/protocolreview/irb

Version: 2.0
Date: 10/05/2009
Approved by: Interim Vice Chancellor for Research
AAHRPP REF#: 122
AAHRPP Elements: I.3.I, II.2.D

POLICY:

- I. Investigators, or other responsible parties, must file either a continuing review application or a final report well in advance of the expiration date of IRB approval.
- II. UIC OPRS strongly recommends submitting the continuing review application or final report application 30-45 calendar days from the date of expiration of IRB approval for expedited non-JBVAMC submissions and 60 calendar days from the date of expiration for expedited JBVAMC submissions. For convened review protocols, investigators are strongly recommended to submit the continuing review or final report application 30-45 calendar days from the date of expiration for non-JBVAMC protocols and 60 calendar days for JBVAMC submissions while also keeping to the submission deadlines for the appropriate board meeting:
<http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/meetings.shtml>
- III. **Responsibility to submit a final report application.** Investigators, or other responsible parties as applicable, must file a UIC OPRS [Final Research Report](#) form to request study closure with OPRS for IRB approved and exempt studies within 30 days of the completion of the study. The term “study closure” refers to IRB-approved studies, while the term “withdrawal” refers to an Initial Review Application or Claim of Exemption that has been submitted but not yet approved by the IRB.
 - A. A UIC OPRS *Final Research Report* form must be submitted even if the research was never initiated, no subjects were enrolled, or the PI is terminating the research earlier than originally planned.
 - B. Once a study has been closed via a UIC OPRS *Final Research Report* form, it cannot be re-opened.
 - C. If a later use for the research data is identified, then the PI must submit a new research application for the use of the previously collected data.
 - D. The later use of the data may qualify for an exemption, if the existing data is recorded without identifiers.
- IV. Department Heads, Unit Heads, and Faculty Sponsors are responsible for ensuring that PIs leaving UIC submit a UIC OPRS *Final Research Report* form for each of their active protocols or transfer the responsibility to another qualified investigator to serve as PI by submitting an amendment form.

- V. PIs who do not file UIC OPRS *Final Research Report* forms may be subject to sanctions, including but not limited to, the classification of the applicable protocol as “lapsed in IRB approval,” determination of research non-compliance, additional education and training, research termination and reporting to appropriate agencies, and/or a limitation of privileges.
- VI. Lapse in IRB approval represents a failure to obtain approval of a final report or obtaining continuing review approval by the expiration date assigned by the IRB. After expiration of IRB approval, all research activities must stop, including any research related interventions, recruitment, data collection, data sharing/reporting and analysis of data, and no new subjects may be enrolled. If a continuing review or final report to the IRB is not received per the timeline in procedure Section II, the research is closed and a new submission is required to re-open it.
- VII. After the IRB approval for a study has lapsed, follow-up interventions or interactions with some or all subjects require the submission of a request to the IRB for a protocol exception. Interventions are allowed to continue only when it is in the best interest of the subjects. To request the continuation of certain aspects of the research, the investigator must submit a UIC OPRS [Protocol Exception](#) form to clearly distinguish and explain what research activities from which he or she will refrain as part of the lapse and what research activities require continuation. The investigator must also explain the underlying reasons for which the protocol exception is requested for each activity and each subject where an over-riding safety concern or ethical issue indicates that it is in the best interests of the individual to continue participating. (Refer to UIC HSPP policy and procedure [Protocol Exceptions](#)). An exception must be requested even if a continuing review application has been submitted. A protocol exception does not replace or represent continuing IRB review of the research.
- VIII. Lapses in IRB approval are considered by UIC policy to represent non-compliance with the Federal regulations and the requirements of the IRB and are handled according to the UIC HSPP policy and procedure, [Handling Complaints and Allegations of Potential Non-Compliance with Human Subject Protection Regulations](#), including consideration of whether the non-compliance is serious and/or continuing. The IRB applies the terms “continuing non-compliance” and “serious non-compliance” as defined in the UIC HSPP policy and procedure [Reporting of Unanticipated problems, Suspensions, Terminations, and Non-Compliance](#).
- IX. Withdrawal of initial submissions of research is an action taken by the IRB to permanently withdraw a proposal after it has been reviewed and given either contingent approval (i.e., modifications required to secure IRB approval) or been deferred, and the investigator has not responded to the IRB’s request within 90 days.
- X. IRB members, OPRS staff, and OVCR staff may use the most effective means of

communication necessary with respect to contacting investigators as to lapse in IRB approval on an as-needed basis. Documentation of oral and written communications must be filed in the protocol file.

PROCEDURE:

I. Study Closure.

- A. A local study or multi-center study where UIC is the lead or coordinating site is eligible for closure if it meets all of the following criteria:
 1. The PI has completed enrollment and data collection;
 2. The PI and his or her research personnel no longer have any contacts or interactions with the subjects, including long-term follow up; and
 3. Analysis of identifiable data is complete and, if a manuscript or presentation is planned, there is no possibility of further data analysis requests (i.e., acceptance of publication or presentation).
- B. The investigator submits the completed UIC OPRS *Final Research Report* form to OPRS for IRB review and approval.
- C. The UIC OPRS *Final Research Report* form may be reviewed via expedited review procedures. (Refer to UIC HSPP policy and procedure, [Expedited Review](#)). The UIC OPRS *Final Research Report* form of research meeting the criteria for exemption (45 CFR 46.101(b)) may be reviewed via exempt review procedures. (Refer to UIC HSPP policy and procedure [Exempt Review of Research](#)).
- D. IRB Chair (or designee) or, for non-VA exempt research, designated OPRS staff reviews the UIC OPRS *Final Research Report* form using the *Final Report to Previously Approved Research* review guide. A communication documenting the IRB's and/or OPRS staff member's determination is generated and sent to the investigator, with copies sent to the Academic Department Head, other relevant UIC oversight committees (e.g., Investigational Drug Service, Radiation Safety, Cancer Center), JBVAMC R&D Committee (if JBVAMC is a performance site), NU OPRS (if NU is a performance site), and the UIC OPRS protocol file. The IRB is notified of the action at the next scheduled meeting via the agenda.

II. Lapse in IRB Approval: Preventative Measures. The OPRS utilizes several measures to prevent a lapse in IRB approval and the resultant non-compliance with Federal regulations and UIC HSPP policies.

- A. Approval letters to investigators include an attachment reminding investigators that they are responsible for ensuring that a continuing review application or final report is submitted to OPRS prior to the expiration date to prevent a lapse of IRB approval.
- B. Investigators receive reminders from OPRS at 90, 60, and 30 days prior to the expiration of the approval period.
- C. The AD for each IRB monitors the status of the board's protocols weekly through the RiSC database management software and ensures reminders are

sent at 90, 60, and 30 days before expiration and that expiration and closure letters are sent after the expiration date.

III. Lapse in IRB Approval: Procedures on the Expiration Date. *The following procedures relate to both Minimal and Greater than Minimal Risk research.*

- A. If the investigator has not submitted and obtained continuing review approval or approval of a final report by the protocol's expiration date, IRB approval lapses.
- B. The investigator is notified of the lapse in IRB approval via e-mail and campus mail by the *Notice of Expiration of IRB Approval* letter. The notification explains the consequences of the lapse (Item C below), contains an attached page to facilitate completion of the information requested in Item E below, and instructs the investigator on when and how to submit a protocol exception request (Item F below). The letter is copied to the Academic Department Head, Faculty Sponsor (if applicable), other relevant UIC oversight committees (e.g., investigational drug service, radiation safety, cancer center), JBVAMC ACOS of R&D (if JBVAMC is a performance site), EC (if the Collaborative IRB/ UIC IRB#4), NU OPRS (if NU is a performance site), ORS (grants and contracts office), sponsor and the UIC OPRS protocol file. This letter is also copied to the OVCR QIP.
- C. Consequences of the lapse are that:
 1. All research activities must stop, including recruitment, research interventions or interactions, data sharing/reporting, data collection and analysis of identifiable data, and no new subjects may be enrolled;
 2. The research may continue only after the investigator receives written approval from the IRB; and
 3. Procedures to close the research are initiated per Sections IV and V of this policy and procedure.
- D. The lapse represents non-compliance and is referred to the IRB according to the UIC HSPP policy, *Handling Complaints and Allegations of Potential Non-Compliance with Human Subject Protection Regulations* for consideration of whether the non-compliance is serious or continuing.
 1. Specifically, the IRB chair or designee makes a determination of whether the lapse represents possible serious or continuing non-compliance.
 2. If the chair or designee determines that the lapse represents possible serious or continuing non-compliance, it is referred to the convened IRB for a final determination.
 3. The compliance determination is communicated to the investigator by e-mail and campus mail. Serious and/or continuing noncompliance is reported to applicable federal regulatory agencies, agency heads, sponsors and institutional officials in accordance with the UIC HSPP policy and procedure on reporting, *Reporting of Unanticipated problems, Suspensions, Terminations, and Non-Compliance*.
- E. The investigator must provide for nonexempt research the following to the IRB in writing within five calendar days of the date of expiration:

1. Number of currently enrolled subjects;
 2. List of subjects for whom stopping research will cause harm; and
 3. Assessment for each of the risk of stopping study activities and the need to continue any research interventions; **OR**
 4. A signed assurance that no subjects are currently enrolled in the research or are at risk if research interventions are stopped.
- F. A form to facilitate communication of this information to the UIC OPRS is provided on page 3 of the *Notice of Expiration of IRB Approval* letter. Submitting the information above or completing and mailing page 3 of the UIC IRB expiration of IRB approval notice letter does not replace the need for the investigator to submit either a continuing review or final report.
- G. When the investigator feels it is in the best interest of a subject to continue research activities during the lapse, a request to continue the subject should be submitted to the IRB using the UIC OPRS *Protocol Exception* form. Based on the information provided by the investigator on the UIC OPRS *Protocol Exception* form, the IRB chair (in consultation with the COS when JBVAMC is a performance site) may decide to allow research interventions and interactions to continue in individual subjects where an over-riding safety concern or ethical issue indicates that it is in the best interests of the individual to continue participating. (Refer to UIC HSPP policy *Protocol Exceptions*.)
- H. The OVCR QIP may perform audits on lapsed protocols to ensure that research activities stopped on the expiration date:
1. At the specific request of the IRB (i.e., protocols that were closed due to investigator non-responsiveness); and/or
 2. As periodic spot audits, as described in the UIC HSPP policy [OVCR Quality Improvement Program - Monitoring and Auditing](#).

IV. Lapse in IRB Approval: Procedures After the Expiration Date for Greater Than Minimal Risk Research.

- A. The investigator must submit a continuing review or final report **within 28 calendar days** after the expiration date. Submission of page 3 of the letter received from OPRS does not replace the need to also submit a continuing review or final report.
- B. The 28-day period does not constitute an extension of the IRB approval period. The period is meant to allow for continuing review or final report submissions that may be in process before procedures to close the research protocol are initiated. Research activities must be stopped during this period, unless a protocol exception has been granted.
- C. **Five (5) Calendar Days after the Date of IRB Expiration.** The investigator must provide the information requested in III. E. to the IRB in writing within five calendar days of the date of expiration.
- D. **Fourteen (14) Calendar Days after the Date of IRB Expiration.**
 1. If the investigator does not respond with the information described in IV.A and IV.B by calendar **Day 14**, a notice is sent by the IRB notifying the investigator that procedures to close the research have been

initiated. The investigator is again reminded of their obligation to submit the documentation described in IV.A and IV.B above.

2. The Department Head or Unit Head is also contacted by the IRB if the investigator does not respond with the information described in IV.A and IV.B by **14 calendar days** after the expiration date. The head is notified of the lapse in IRB approval and reminded of their responsibility for the conduct of the research due to the lack of response from the investigator. As a result, the department or unit head must attest to the IRB in writing that there are no active subjects, potential risks to prior subjects, or outstanding obligations to subjects. If these conditions are not known or not true, it is the responsibility of the Department Head or Unit Head to appoint a qualified PI to ensure the safety, rights and welfare of the subjects have been protected and to provide the IRB with details of the subjects' status. **The Department Head is given 14 days to provide this information to the IRB.** Once this information is obtained, the IRB decides on the disposition of the research (e.g., close the research, re-assign to another investigator).
3. If the continuing review or final report has been submitted by **14 calendar days** after the expiration date but not yet reviewed or the approval letter not yet sent, the communications described in 1 and 2 above are not sent to the investigator and Department Head.

E. Twenty-eight (28) Calendar Days after the Date of IRB Expiration.

1. If the investigator has not submitted a continuing review or final report by 28 calendar days after the expiration date, **the research is closed on calendar Day 28 by the IRB** unless the IRB chair (in consultation with the COS when the JBVAMC is a performance site) has decided it is in the best interest of individual subjects for research interactions or interventions to continue.
2. The IRB/OPRS sends a letter via email and campus mail to the investigator on **Day 28** after the expiration date indicating that there has been a lapse in IRB approval and the research has been closed. Copies of this communication are provided to the Department or Unit Head, HPA, Faculty Sponsor (if applicable), other relevant UIC oversight committees (e.g., investigational drug service, radiation safety, cancer center), JBVAMC ACOS of R&D (if JBVAMC is a performance site), EC (if UIC IRB#4), NU OPRS (if NU is a performance site), ORS (grants and contracts office), sponsor and the UIC OPRS protocol file.
3. A separate letter indicating that the research has been closed is addressed to the Department or Unit Head.
4. The IRB Chair makes a compliance determination and decides whether the failure to respond to the lapse notice represents serious or continuing noncompliance. If the chair or designee determines that the lapse represents possible serious or continuing noncompliance, it is referred to the convened IRB for a final determination. The compliance determination is communicated to the investigator by e-mail and

campus mail. Serious or continuing noncompliance is reported to applicable federal regulatory agencies, agency heads, sponsors and institutional officials in accordance with the UIC policy on reporting - Reporting of Unanticipated problems, Suspensions, Terminations, and Non-Compliance.

5. Copies of the study closure letter to the investigator are forwarded to the institutional official.
 6. UIC OPRS will notify UIC's grants and contracts office and the JBVAMC R&D Committee (if applicable) of the lapse in IRB approval.
- F. Investigators who have not corrected the lapse in protocol approval before 28 days are not allowed to submit further research for initial review until the lapse in IRB approval has been addressed and lapse compliance training has occurred.
- G. If the investigator has submitted a continuing review or final report before the expiration date and/or the investigator demonstrates a good faith effort in working toward obtaining IRB approval of the continuing review or final report, the IRB chair or designee may at their discretion postpone the closure of the study. The Chair must document in writing his or her decision to extend the time to closure. The IRB Assistant Director or IRB Coordinator must ensure that documentation of the above decision is filed appropriately.

V. Lapse in IRB Approval: Procedures After the Expiration Date for Minimal Risk Research.

- A. The investigator must submit a continuing review or final report **within 28 calendar days** after the expiration date. Submission of page 3 of the letter received from OPRS does not replace the need to also submit a continuing review or final report.
- B. The 28-day period does not constitute an extension of the IRB approval period. The period is meant to allow for continuing review or final report submissions that may be in process before procedures to close the research protocol are initiated. Research activities must be stopped during this period, unless a protocol exception has been granted.
- C. **Five (5) Calendar Days after the Date of IRB Expiration.** The investigator must provide the information requested in III. E to the IRB in writing within five calendar days of the date of expiration.
- D. **Twenty-eight (28) Calendar Days after the Date of IRB Expiration**
 1. If the investigator has not submitted a continuing review or final report by 28 calendar days after the expiration date, **the research is closed on calendar Day 28 by the IRB** unless the IRB chair (in consultation with the COS when the JBVAMC is a performance site) has decided it is in the best interest of individual subjects for research interactions or interventions to continue.
 2. The IRB sends a letter via email and campus mail to the investigator on **Day 28** after the expiration date indicating that there has been a lapse in IRB approval and the research has been closed. Copies of this communication are provided to the Department or Unit Head, HPA,

- Faculty Sponsor (if applicable), other relevant UIC oversight committees (e.g., investigational drug service, radiation safety, cancer center), JBVAMC ACOS of R&D (if JBVAMC is a performance site), EC (if UIC IRB#4), NU OPRS (if NU is a performance site), ORS (grants and contracts office), sponsor and the UIC OPRS protocol file.
3. A separate letter indicating that the research has been closed is addressed to the Department or Unit Head.
 4. The IRB Chair makes a compliance determination and decides whether the failure to respond to the lapse notice represents serious or continuing noncompliance. If the chair or designee determines that the lapse represents possible serious or continuing noncompliance, it is referred to the convened IRB for a final determination. The compliance determination is communicated to the investigator by e-mail and campus mail. Serious or continuing noncompliance is reported to applicable federal regulatory agencies, agency heads, sponsors and institutional officials in accordance with the UIC policy on reporting, *Reporting of Unanticipated problems, Suspensions, Terminations, and Non-Compliance*.
 5. Copies of the study closure letter to the investigator are forwarded to the institutional official.
 6. UIC OPRS will notify UIC's grants and contracts office and the JBVAMC R&D Committee (if applicable) of the lapse in IRB approval.
- E. Investigators who have not corrected the lapse in protocol approval before 28 days are not allowed to submit further research for initial review until the lapse in IRB approval been resolved and lapse compliance training has occurred.
- F. If the investigator has submitted a continuing review or final report before the expiration date and/or the investigator demonstrates a good faith effort in working toward obtaining IRB approval of the continuing review or final report, the IRB chair or designee may at their discretion postpone the closure of the study. The Chair must document in writing his or her decision to extend the time to closure. The IRB Assistant Director or Coordinator must ensure that documentation of the above decision is filed appropriately.

VI. Withdrawal of Research.

- A. The modification and deferral letters sent by the IRB to investigators following convened or expedited review of an initial submission indicate the 90 day period for the investigator to respond to the IRB's request. Specifically the letter notes that a reminder letter will be sent if no response is received within 60 days and 30 days later the submission will be withdrawn from the review process and the IRB will not take any further action.
- B. The AD for each IRB monitors the status of the board's protocols weekly through the RiSC database management software and sends reminders at 60 days after the modification or deferral letters were originally sent if no response to the IRB's requests has been submitted.
- C. If no response to the IRB's requests has been submitted by 90 days after the modification or deferral letters were originally sent, the submission is

withdrawn from the review process and no further action is taken. The withdrawal is communicated to the investigator.

REFERENCES:

[21 CFR 50.25\(b\)\(5\)](#), [21 CFR 56.108\(b\)\(2\)](#)
[38 CFR 16.103\(b\)\(5\)\(i\)](#), [38 CFR 16.116\(b\)\(5\)](#)
[45 CFR 46.103\(b\)\(5\)\(i\)](#), [45 CFR 46.116\(b\)\(5\)](#)
[OHRP Guidance on Reporting Incidents to OHRP](#)
[VHA Handbook 1200.05](#)

REVISION LOG:

Version (#, date)	Replaces (#, date)	Summary of changes
1.1, 11/05/08	1.0, 10/01/08	Clarifies the procedures for lapses in approval
1.2, 03/28/09	1.1, 11/05/09	Clarification of the procedure for closing research for lapses in IRB approval
2.0, 10/05/09	1.2, 03/28/09	Significant changes to the time period and general procedures for closing research for lapses in IRB approval. Re-structuring and re-drafting of the procedure portion.