COMIRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur as long as the research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.

A COMIRB determination of the approval period and the need for additional supervision and/or enrollment is made by the COMIRB on a protocol-by-protocol basis. For example, for an investigator who is performing particularly risky research, or for an investigator who has recently had a protocol suspended by the COMIRB due to regulatory concerns, an on-site review by the Office of Regulatory Compliance might occur or approval might be subject to an audit of study performance after a few months of enrollment, or after enrollment of the first several subjects.

For each initial or continuing approval, the COMIRB will indicate an approval period with an approval expiration date specified. COMIRB approval is considered to have lapsed one second after 23:59:59 of the expiration date listed.

For a study approved by the convened panel, the approval period starts on the date that the panel conducts its final review of the study; that is, the date that the convened panel approved the research or the date the convened panel approved with minor modifications (for non-substantive issues). For example, if the protocol was reviewed on April 1, 2008 at full board but received minor modifications which were approved by the panel Chair on May 1, 2008, the expiration date will be March 31, 2009.

For a study approved under expedited review, the approval period begins on the date the COMIRB Chair or COMIRB panel member(s) designated by the Chair gives final approval to the protocol for a maximum period of one year. For example, if the protocol was reviewed on April 1, 2008 by the expedited reviewer but received minor modifications which were approved by the panel Chair on May 1, 2008, the expiration date will be April 30, 2009.

The approval date and approval expiration date are clearly noted on all COMIRB certifications sent to the PI and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of an amendment in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply an amendment to it.
The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of COMIRB approval. Therefore, continuing review and re-approval of research must occur by 23:59:59 of the listed expiration date to avoid study expiration.

1.1 Full-Board Review at Continuing Review

To assist investigators, the COMIRB Office staff will send out renewal notices to investigators 75 days and 45 days in advance of the expiration date; however, it is the investigator’s responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

In conducting continuing review of research not eligible for expedited review, each panel member receives and reviews, at minimum, the following documentation (please note that some items may not require submission from the PI if they are already easily accessed by reviewers within the electronic system):

- the annual continuing review form (with every continuing review), including:
  - summary of gender and demographic status of subjects enrolled to-date;
  - number of subjects considered as members of specific vulnerable population enrolled to-date
- the currently approved COMIRB Application form (with every continuing review);
- the currently approved research protocol (with every continuing review);
- any existing, last or currently approved consent/parental permission/assent form(s)
- any existing, currently active HIPAA compliance forms if the study continues to enroll subjects.
- other adverse events, untoward events or outcomes experienced by subjects reported in summary or table form since last continuing review (if there is a safety oversight body appointed for a multi-center study, a report from this body plus a summary of local adverse events and protocol deviations may be submitted);
- any relevant recent literature
- any relevant multi-center trial reports
- if UCD or one of the affiliates is the lead site of a multi-site study, IRB approvals from other engaged sites on the study.
- For VA research only: An indication from the PI (on the continuing review form) certifying that all subjects entered onto the master list of subjects for the study signed an informed consent form prior to undergoing any treatment interactions or interventions, unless the COMIRB has granted a waiver of informed consent or a waiver of documentation of informed consent. This statement is considered signed by the PI submitting the continuing review through the eRA system, or by attesting to the continuing review submission (see section 25.2.3).
- Note that any amendments to currently-approved documents will be reviewed as a separate amendment submission, but may be reviewed at the same time as a continuing review.

In conducting continuing review of research not eligible for expedited review, all panel members are provided and review all of the above material. For continuing review of research by a convened IRB panel, the primary reviewer leads the panel through the completion of the regulatory criteria for approval in the “COMIRB Primary Reviewer Checklist” plus the continuing review addendum and any other additional checklists appropriate to the study (e.g., device checklist, decisionally challenged checklist, children and neonate checklists).

COMIRB staff attends the convened meetings. The COMIRB staff will retrieve any additional related materials that panel members request from the paper protocol file.

CP-005 Continuing Review of Active Protocols
Effective 3-29-2016
In the case of expedited review, the Chair (or an experienced reviewer designated by the Chair from the IRB members) may request the COMIRB office staff provide them with any additional materials required for the review.

Review of currently approved consent documents must occur during the scheduled continuing review of research by the COMIRB, but informed consent documents must also be reviewed whenever new information becomes available that would require modification of information in the informed consent documents.

1.2 Expedited Review at Continuing Review

In conducting continuing review under expedited review, the reviewers receive all of the above material. The reviewer(s) complete the Continuing Review Addendum Checklist and/or the COMIRB Primary Reviewer Checklist, and any other additional checklists appropriate to the study, to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

Typically, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in specific circumstances including:

- Reviews described by expedited review categories (8) or (9) at 63 FR 60364-60367 (see Expedited Review Categories).
- Circumstances where COMIRB requires initial review at full board (e.g., prisoner research, genetic analyses, device risk determinations, or research with unclear risks), but the full committee determines that future reviews may be expedited under categories (1) through (7) at 63 FR 60364-60367.

It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review. If so, the investigator may be granted additional time to resubmit a full-board application to COMIRB before the application is withdrawn, but the approval may still lapse and the study expires.

1.3 What Occurs if there is a Lapse in Continuing Review

The COMIRB and investigators must plan ahead to meet required continuing review dates. If the COMIRB has not reviewed and approved a research study by the end of the approval period specified by the COMIRB, all research activities must stop, including recruitment (media advertisements must be pulled and no new subjects may be enrolled), enrollment, consent, interventions, interactions, data collection, and data analysis, unless the COMIRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. This will occur even if the investigator has provided the continuing information before the expiration date, as continuation of research after expiration of COMIRB approval is a violation of the regulations. Therefore, investigators must allow sufficient time for COMIRB review before the expiration date. Retrospective approval for work done after the expiration date cannot be granted. If there is any concerns in regards to subjects’ safety and welfare caused by discontinuation of research activities, investigators must contact the COMIRB Director to obtain written permission to continue such activities that affect subjects’ safety and welfare (see below for detail).

An expiration letter (or email) will be sent to investigators at the end of the approval period. The expiration letter is sometimes sent the day before or after expiration (e.g., when the expiration date falls on a weekend), but the letter will always clearly show the date of expiration.

Failure to submit continuing review information on time is noncompliance and will be handled according to the noncompliance policy.

CP-005 Continuing Review of Active Protocols
Effective 3-29-2016
If the investigator is actively pursuing renewal with the COMIRB and the COMIRB believes that an
over-riding safety concern or ethical concern is involved, a request to continue current research
subjects can be made BUT enrollment of new subjects is not permitted.

- All requests from investigators to continue current subjects in research procedures must be
  submitted in writing to the COMIRB Director. The COMIRB Director, in consultation with the
  panel Chair as needed, determines which procedures, if any, may be performed because
  stopping those research procedures will pose a potential harm to subjects or cause an
  over-riding ethical concern. The COMIRB Director provides a written response listing the
  research procedures that may be continued because lapse of those procedures would
  cause harm.
- Communications regarding permission to continue research procedures during expiration
  are logged in the User Log section of the Summary page in eRA(InfoEd). A written
  communication of such permission obtained by the investigator from the COMIRB Director
  (e.g., email communication) must be filed in the appropriate study file.
- The permission to continue certain research procedures during a period of expiration is
  contingent upon a good faith effort of the investigators to work toward re-approval of their
  research by COMIRB. Failure to put forth a good faith effort may result in loss of the
  permission to continue certain research procedures.

Once the study approval has expired, COMIRB re-review and re-approval must occur before the study
can resume. The COMIRB cannot retrospectively grant approval to cover a period of lapsed IRB approval.

**For EASTERN COLORADO HEALTH CARE SYSTEM research, if approval expires:**

1) The local research office is responsible for promptly notifying the investigator. COMIRB will
   also send an expiration letter.
2) The investigator must: a) Stop all research activities including, but not limited to, enrollment
   of new subjects; continuation of research interventions or interactions with currently
   participating subjects; and data analysis; b) Immediately submit to the Research Office a list
   of research subjects who could be harmed by stopping study procedures; c) Immediately
   submit to the COMIRB Director information outlining which type of subjects currently enrolled
   could be harmed by stopping study procedures.
3) The COMIRB Director will coordinate with the appropriate IRB Chair, as needed to
   determine if subjects on the list may continue participating in the research interventions or
   interactions.
4) The sponsoring agency, private sponsor, the Affiliate(s), the VA Office of Research and
   Development (ORD), the regional VA Office of Research Oversight (ORO), or other Federal
   agencies must be informed, as appropriate.
5) Once the study approval has expired, COMIRB re-review and re-approval must occur
   before the study can resume. The COMIRB cannot retrospectively grant approval to cover a
   period of lapsed IRB approval.