Department:	**UAMS Institutional Review Board**
Policy Number:	**7.6**
Section:	**Procedures for Study Review**
Effective Date:	**July 31, 2002**
Revision Date:	**February 5, 2005; June 1, 2005; March 8, 2008; July 28, 2008; January 24, 2011; March 11, 2011; August 30, 2018; January 19, 2019; August 16, 2021**

SUBJECT: Continuing Review

POLICY

Periodic review of all human research activities allows the IRB to determine whether the risk/benefit ratio has changed, there are unanticipated problems involving risks to subjects, and any new information regarding the risks and benefits should be provided to subjects.

The IRB must conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk. The IRB must decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects. The IRB must review each FDA-regulated study at least once per year and can require more frequent reviews.

PROCEDURE

A. The IRB e-system is designed to send reminder emails to the study's Principal Investigator and Primary Contact listed in the e-system approximately 12, 8, and 4 weeks prior to the project's continuing review expiration date with a suggested return deadline. However, study teams should not rely solely on the e-system emails. Study teams retain responsibility for submitting and receiving continuing review approval on time. Sufficient time should be allowed for processing the report and IRB approval prior to the project's expiration.

B. IRB approval letters shall include the expiration date of continuing review.

C. The expiration date is the last date on which study activities may occur.

D. The expiration date may change from year to year, as the study calendar resets to the date of the meeting at which the convened IRB conducts continuing review for full-board studies. The following are examples of expiration date determinations for studies the IRB has determined require continuing review annually.

E. The following are scenarios for determining the date of continuing review expiration
   1. Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on October 1, 2010. Continuing review must occur within 1 year of the convened meeting date of the meeting, so the expiration date is September 30, 2011.

   2. Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2010, and approves the protocol contingent on specific minor conditions the IRB chair/designee can verify. On October 31, 2010, the IRB chair/designee confirms the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting reviewed and approved the protocol. Since the changes did not require review by the convened IRB, the expiration date is September 30, 2011.

   3. Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2010, which requires major revisions or is tabled. The study is reviewed at subsequent convened meetings on October 15 and October 29, 2010. At the October 29, 2010 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the last convened meeting at which the IRB reviewed and approved the protocol, so the expiration date is October 28, 2011.

F. Failure to submit a timely continuing review will result in approval expiration. If the IRB has not reviewed and approved a study by the continuing review expiration date, all research activities must stop. No new subjects may be recruited or enrolled.

1. Interventions and interactions with current subjects must stop. If the Investigator believes there are current subjects whose safety might be at risk by stopping all procedures, the Investigator must contact the IRB immediately upon expiration notice. Interventions and interactions with current subjects may only then occur if the IRB finds an over-riding safety concern or ethical issue involved that makes it in the best interests of individual subjects to continue participating in the research interventions or interactions. Only an IRB Chair may authorize this continued interaction. Investigators may not make this decision. No other research activities may be authorized by the IRB Chair.

2. Generally, study expirations do not need to be reported to regulatory agencies. However, a pattern of study expirations may indicate non-compliance and will be reviewed and classified as per IRB Policies 12.5 and 12.6.

G. **Submission Requirements for Continuing Review Form:** For all studies undergoing review by the convened IRB, the Investigator must provide the following:

1. A completed Continuing Review Form in the e-system. This form requires the number of subjects accrued, withdrawn and reasons for withdrawal. See IRB Policy 14.5 for accrual and enrollment definitions. The form also requires a summary of activity since the last IRB review. Activities to be summarized include:
   a. Adverse events and adverse outcomes experienced by subjects;
   b. Unanticipated problems involving risks to participants/others;
   c. Complaints about the research and resolution thereof
   d. Relevant recent literature
   e. Interim findings
   f. Relevant multi-center trial reports
   g. Current risk-benefit assessment based on study results to date

H. IRB Review Process and when full IRB review is not required

1. Convened IRB. For all studies requiring review by the convened IRB, the processes outlined in IRB Policy 7.4 will be followed.

2. Exceptions to Continuing Review Requirement

a. Unless the IRB determines and documents otherwise, continuing review of research initially approved after Jan. 20, 2019, is not required in the following circumstances:
   i The research is eligible for expedited review as per IRB policy 7.5, Expedited Review.
   ii The research was reviewed by the IRB in accordance with Limited IRB review as per IRB policies 7.3, Exempt Categories of Research and 7.12, Limited IRB Review.
   iii The research was reviewed by the IRB as per IRB policy 7.14, Equivalent Protections Using Flexible IRB Review Processes.
   OR
   iv Research initially determined to be “greater than minimal risk” has progressed to the point that it involves only one or both of the following, which are part of the IRB approved study.
   - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
   - Accessing follow up clinical data from procedures that subjects would undergo as part of clinical care.

b. The IRB must document the rationale for conducting continuing review if any of the above conditions are met. Issues that may prohibit release from Continuing Review include but are not limited to the following situations:
   i Require additional regulatory or ancillary oversight (COI, new findings, etc.)
   ii FDA regulated studies. Note that FDA-regulated research initially reviewed by the convened board may undergo continuing review using expedited procedures under certain conditions, as described in FDA guidance.
   iii Research conducted internationally or at non-UAMS sites
   iv History of non-compliance

c. For studies for which full continuing review is not required, the study team must still:
   i Submit modifications for project changes;
   ii Report RNI's;
   iii Close the study once it ends, or when personal identifiers are removed from the data/biospecimens and all codes and keys are destroyed.
   iv Submit an abbreviated annual update form to the IRB, limited to asking whether the PI wishes for the study to remain open, whether anything on the study has changed, and an update on enrollment status.

REFERENCES

45 CFR 46.109(e) and (f)
21 CFR 56.109(f)
AAHRPP Element II.2.E
OHRP Continuing Review Guidance (2010)
FDA Guidance Titled *IRB Continuing Review after Clinical Investigation Approval*