Department: **UAMS Institutional Review Board**
Policy Number: **7.6**
Section: **Procedures for Study Review**
Effective Date: **July 31, 2002**
Revision Dates: **February 8, 2005; May 13, 2004; October 11, 2002**

SUBJECT: Continuing Review

Policy: The IRB must conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk, but not less frequently than once *per* year. The IRB should decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects.

Periodic review of all human research activities is necessary to determine (1) whether the risk/benefit ratio has changed, (2) whether there are unanticipated findings involving risks to subjects, and (3) whether any new information regarding the risks and benefits should be provided to subjects. All non-exempt research protocols must be periodically reviewed, not less than one time per year, in accordance with this policy.

Studies deemed as Exempt will be asked to complete an Annual Update form. See Policy 7.3.

As a service, ARIA automatically emails continuing review expiration notices at approximately 8 and12 weeks prior to the project's continuing review expiration date with a required return deadline. However, this service should not be seen as assuming any duty that an investigator retains 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.

Failure to submit a timely continuing review will result in expiration of the protocol. There is **no grace period** extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date can not be granted. If the IRB has not reviewed and approved a research study by the continuing review expiration date, ARIA sends out an automatic expiration letter stating that all research activities, including procedures with/on current participants and data analysis, must stop.

Only upon a finding by the IRB that it is in the best interests of individual subjects to continue participating in the research interventions or interactions, may any research activity continue after CR expiration. Investigators may not make this decision. Enrollment of new subjects cannot occur after the expiration of IRB approval.

If continuing review expires on a drug/device study, the involved Pharmacy contact will be notified.

This type of study expiration does not need to be reported to OHRP under DHHS regulations. (Note: If a study is actively suspended or terminated by a convened IRB meeting, OHRP must be notified.)

Process:

1. Regardless of continuing review by expedited or full IRB processes, the **Investigator** must provide:

    a. A completed ARIA continuing review application;
    b. Informed Consent Document – ARIA automatically loads the currently approved consent document, if applicable, into the CR form. The Investigator MUST verify the accuracy of what is listed and correct if inaccurate.
    c. In addition to answering yes/no or proving a number in the ARIA form, a status report for all events since the last report should be submitted that includes a summary of the following:
        i. All adverse events,
        ii. Unanticipated problems involving risks to participants/others,
        iii. Complaints about the research and resolution thereof
        iv. Relevant recent literature
        v. Interim findings
        vi. Relevant multi-center trial reports
        vii. Participant benefits
        viii. Current risk-benefit assessment based on study results to date
        ix. Gender, Minority status, and Vulnerable Population status and description
        (Example: Female, Caucasian, Prisoner)
        This may be provided in Step 10 of the form, or in a separately uploaded document.
        x. Reports from Data Safety Monitoring or IND Monitoring Activities required in policy 7.8.
    d. If an Investigator allows a study to expire before continuing review approval is received, the investigator must immediately provide the IRB with a list of current participants whose safety might be at risk by stopping research procedures. If the research involves CAVHS, the Investigator must also notify the R&D Committee Chair.

2. IRB Committee Operations

A. Primary Reviewer System. When a protocol is reviewed for continuing review at the IRB Committee, a primary reviewer system will be used. All reviewers will have access to the complete study file. The Primary Reviewer will be responsible for reviewing the study and making sure the requirements of this policy are met. However, the full IRB Committee will discus the protocol and make determinations for vote.

The following applies to Research reviewed by the Full IRB Committee or Research reviewed under Expedited Procedures.

B. Approval Criteria: The criteria for granting continuing review approval is the same as for initial review, as outlined in Policy 7.1. The Primary Reviewer must look to see that:

1. Risks continue to be minimized and reasonable in relation to the benefits,
2. Selection of subjects is still equitable
3. Informed consent is being obtained and documented appropriately
4. As applicable, provisions for monitoring of the data are still appropriate to ensure the safety of the subjects
5. As applicable, provisions to protect subject privacy and data confidentiality are adequate
6. Safeguards for vulnerable populations, as applicable, are still adequate

C. Documentation of Approval Period. The IRB must determine which protocols require continuing review more often than annually, as appropriate to the degree of risk and as necessary to ensure the continued protection of the rights and welfare of research subjects. See Policy 16.1 for detailed risk-benefit analysis. Studies with a high risk and low probability for benefit may require approval periods of greater than just once a year. The following are examples of studies that may need additional review:

a. Involvement of vulnerable populations;
b. Research conducted internationally;
c. The involvement of recombinant DNA or other types of gene transfer protocols;
d. The use of waiver of informed consent procedures, e.g. surrogate consent;
e. Classified research;
f. Research for which subjects would be exposed to additional risks, e.g. breach of confidentiality, continual non compliance with federal regulations, Phase 1 studies, disproportionate number or severity of SAEs;
g. Previous suspension of the researcher due to compliance, record-keeping or other concerns
h. Recommendations from other intra-institutional committees

D. Verification from Outside Source. The IRB should also determine if verification from an outside source is needed regarding the study. Studies with very complex protocols with unusual risks or protocols being conducted by investigators who have failed to respond to other Chair or Committee requirement are examples of when the IRB might request verification from an outside source that no material changes have occurred since the previous review.

E. Continuing review for a research protocol will be subject to **full IRB review** each approval period, **unless:**

1. Originally reviewed under expedited procedures; or
2. Research is permanently closed to the enrollment of new subjects, all subjects have completed all research related interventions and the research is to remain open only for long-term follow-up of subjects; or
3. No subjects have been enrolled and no additional risks have been identified; or
4. The remaining research activities are limited to data analysis.

When any of the above conditions are met, the IRB may determine that review should occur through expedited processes.

F. Expiration of CR. The IRB Chair or Committee must determine whether there is an over-riding safety concern or ethical issue such that the interests of individual participants would be best served by continuing with the research interventions or interactions. In CAVHS research, the Chair or Committee should consult with the R&D Committee Chair.

G. Review of the Consent Document. Review of the currently approved consent document must ensure that the information is still accurate and complete. 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. Review of currently approved or proposed consent documents must occur during the continuing review but may be done more frequently if new information becomes available.

H. Review of New Amendments to Protocol Submitted at Time of Continuing Review. Amendments and addenda to a research protocol may be submitted at the time of continuing review. A separate cover letter describing the change and all appropriate tracked or highlighted documentation (examples include consent form, protocol, brochures) must accompany the continuing review application. The amendments may not be implemented by an investigator prior to review and approval by the IRB Committee.

I. Summary Status Report Must be reviewed in light of Approval Criteria. Continuing review responsibilities include reviewing reports of adverse reactions and unexpected events involving risks to subjects or others.

J. Continuing Review Date Determinations. Several scenarios for determining the date of continuing review apply for protocols reviewed by the IRB at a convened meeting. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

> Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on October 1, 2002. Continuing review must occur within 1 year of the date of the meeting, that is, by October 1, 2003.
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> Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2002, and approves the protocol contingent on specific minor conditions the IRB chair or his/her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol, that is, by October 1, 2003.
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> Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2002, which requires major revisions or is tabled. The study is reviewed at subsequent convened meetings on October 15 and October 29, 2002. At their October 29,

2002 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the convened meeting at which the IRB reviewed and approved the protocol, that is, by October 29, 2003.

The continuing review expiration date may change from year to year. Each time the convened IRB conducts continuing review, the study calendar is reset to the date of that meeting.

Example: A study's continuing review date expires on June 1, 2000. The IRB convened on May 15, 2000 and granted protocol approval. The next continuing review approval will expire on May 15, 200l.