

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that research activities be periodically reviewed at intervals appropriate to the degree of risk, but not less than once per year as required by the Federal regulations.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. 45 CFR 46.109(e)

B. 45 CFR 46.110

C. OHRP Guidance on Continuing Review, July 11, 2002

D. 21 CFR 56.109

IV. Definitions

A. **Continuing Review:** Periodic review of research activities necessary to determine whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, and whether any new information regarding the risks and benefits should be provided to participants.

B. **Exempt Review:** Studies determined by the IRB to meet the exempt criteria as defined by the Federal regulations. Exempt studies do not require periodic review by the IRB unless a change in the project is planned.

C. **Expedited Review:** Studies determined by the IRB to meet the expedited criteria as defined by the Federal regulations.

D. **Not Less Than Once Per Year:** All research proposals, with the exception of exempt proposals, must receive IRB continuing review at a minimum of once every 365 days, per Federal regulations. There are no exceptions or grace periods allowed.

F. **Standard Review:** Studies reviewed by the full, convened IRB Committee with a recorded vote and corresponding minutes to document the discussion.

V. Procedures

A. Types of Review

1. Standard review

- a. Research protocols initially reviewed by the full convened IRB Committee are reviewed using standard review procedures unless the study has been modified such that it can be reclassified as eligible for expedited review, as defined in the Federal regulations (See IRB Policy, IRB Review – Expedited Review).
- b. Research activities that previously met criteria for exempt or expedited review may change such that standard review would be required. This change in review criteria is prompted at the time of continuing review or review of an amendment.
 - (1) **Primary Reviewer System.** When conducting continuing review at a full IRB Committee, the IRB Committee uses a primary reviewer system for continuing review. However, the full IRB Committee is informed of the Reviewer's findings at a convened meeting. Primary reviewers receive and review a copy of the complete protocol including any modification previously approved by the IRB Committee and any monitoring or audit reports conducted since the last review. Even when using a primary reviewer system, the full, convened IRB Committee discusses the protocol and makes a determination with a recorded vote.

2. Expedited Review

- a. When conducting research under an expedited review procedure, the IRB Committee Chair or designated IRB Committee Member conducts the review on behalf of the full IRB Committee.
- b. Research protocols that were originally reviewed using expedited review procedures may receive continuing review on an expedited basis, unless previously met criteria have changed since the previous IRB review and approval.
- c. Research protocols that were originally reviewed by the full, convened IRB Committee but currently meet the following criteria may receive expedited review by the IRB:
 - (1) The research is permanently closed to the enrollment of new participants; and
 - (2) All participants have completed all research-related interventions; and
 - (3) The research remains active only for long-term follow-up of participants; or

- (4) No participants have ever been enrolled at any site and no additional risks have been identified; or
- (5) The remaining research activities are limited to data analysis.

3. Exempt Research Activities

- a. Exempt studies do not require completion of annual reviews; however, any changes to the research proposal are submitted to the IRB for approval before implementation.
- b. Amendments to Exempt protocols are reviewed and approved by an IRB Administrator or Assistant Administrator. However, if the amendment affects the status of the protocol review level, it goes to the IRB Chair or the designated IRB Committee Member for review and determination at the appropriate review level (i.e. Expedited or Standard review).

B. IRB Continuing Review Criteria

- 1. Continuing review must be substantive and meaningful. The approval criteria for continuing review are the same as that for initial review (See IRB Policy, IRB Review – Full Committee). Therefore, it is the responsibility of the IRB to determine that:
 - a. Risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
 - b. Selection of subjects continues to be equitable;
 - c. Informed consent continues to be appropriately obtained and documented;
 - d. Adequate provisions for monitoring the data collected to ensure the safety of the subjects are provided, when appropriate;
 - e. Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, are provided, when appropriate; and
 - f. Appropriate safeguards for vulnerable populations are provided.
- 2. The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:
 - a. Protocols randomly selected by the IRB Office

- b. Complex protocols involving unusual levels or types of risks to participants;
 - c. Protocols conducted by PIs who previously have failed to comply with Federal regulations or the requirements or determinations of the IRB; and/or
 - d. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.
3. To allow adequate time for IRB review and to avoid any unnecessary delays, the Principal Investigator (PI) provides an "Application for Continuing Review" to the IRB 60 days prior to the IRB expiration date. The "Application for Continuing Review" includes a status report on the progress of the research, including:
- a. The maximum number of participants previously approved by the IRB to be *consented* by the PI for the life of the study;
 - b. The total number of participants *consented* by the PI to participate to date (including any withdrawals by participant, PI or sponsor OR consented screen failures);
 - c. The total number of participants *consented* by the PI since the previous IRB continuing review approval (including any withdrawals by participant, PI or sponsor OR consented screen failures). In addition, the PI should include:
 - (1) How many of these participants completed the study (participated in the study beyond screening); and
 - (2) How many of the participants consented were withdrawals (including the total for the entire duration of the study).
 - d. A *summary* of the following activities that have occurred since previous IRB continuing or initial review:
 - (1) Any adverse events and a profile of what differed from initially expected;
 - (2) Any Data and Safety Monitoring reports;
 - (3) Any events requiring reporting to the IRB (e.g., unanticipated problems and unexpected serious adverse events);

- (4) Any unanticipated problems involving risks to participants or others, even at sites in which the Investigator is not responsible for the conduct of the research;
 - (5) Any participant withdrawals
 - (6) Any participant complaints;
 - (7) Any recent relevant literature;
 - (8) Any interim findings;
 - (9) Any progress reports;
 - (10) Any multicenter reports;
 - (11) Any other relevant information, especially that may impact the risk/benefit ratio;
 - (12) Any problems recruiting potential participants; and
 - (13) Any benefits from the research.
- e. A copy of the current, IRB stamped, approved, informed consent documents as well as an unstamped copy of the informed consent document to be stamped with new continuing approval dates.
4. **Informed Consent Documents (ICDs).** Review of the currently approved ICD must ensure that the information is still accurate and complete. Any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated ICD. Review of currently approved or proposed ICDs occur during the scheduled continuing review of research by the IRB, but may be done more frequently if new information becomes available.
 5. **New Amendments to Protocol Submitted at Time of Continuing Review.** Amendments or revisions to a research protocol may be submitted at the time of continuing review. A "Request for Amendment" and all appropriate documentation accompany the "Application for Continuing Review." The amendment or revision is not implemented by an Investigator prior to review and approval by the IRB.
 6. **Cooperative Protocol Research Program (CPRP) Protocols.** Continuing IRB review is required as long as individually identifiable follow-up data are collected on participants enrolled in DHHS-supported Cooperative Protocol Research Program (CPRP) protocols. This remains the case even after a protocol has been closed to enrollment at all sites and protocol-related intervention has been completed for all participants, even if research is limited to final data analysis.

7. Continuing Review of Data Safety Monitored (DSM) Clinical Trials. When a multi-site clinical trial is subject to oversight by a DSM, the IRB may rely on the most recent report(s) from the DSM indicating that it has reviewed study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring individual, non-DOH adverse event reports, along with any other information needed to ensure that its continuing review is substantive and meaningful.

C. IRB Approval of Continuing Review

1. The IRB conducts continuing review of all research proposals, with the exception of research that meets the criteria as Exempt, at intervals appropriate to the degree of risk, but not less than once per year.
 - a. Standard Review. Research that meets the criteria for standard review is reviewed within one year of the date of the full, convened IRB meeting at which the research was approved (with or without specific revisions) even though the research activity may not begin until after IRB final approval is granted. For example, at the January 5, 2003 full, convened IRB meeting a proposal is granted "approval pending minor modifications" with a 12 month approval period. The Investigator provides an adequate response to the Committee Action Letter (CAL) on April 10, 2003, after review by the Chair or designated IRB Member, final approval is extended. The continuing review date for this proposal will be January 4, 2004. All research activities cease on the expiration date.
 - b. Expedited Review. Research that meets the criteria for expedited review is reviewed within one year of the date that final approval was granted by the IRB Chair or designated IRB Committee Member.
2. Research may be restricted, modified, or halted altogether based on continuing review by the IRB Committee. A pending or deferred status is given to all studies in which the IRB requests changes to current documents during Continuing Review. IRB approval is not granted until all requested changes to previously approved documents are completed by the Investigator, and reviewed and approved by the IRB. This does not extend the expiration period.
3. Based on the IRB continuing review, previously imposed restrictions may be relaxed or additional restrictions may be imposed.


D. Expiration of IRB Approval

1. There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Therefore, the study expires and extensions beyond the expiration date are not granted.
2. If the IRB does not re-approve the research by the specified expiration date, study activities must cease, pending re-approval of the research by the IRB. The full IRB Committee suspends the study and follows the requirements of suspension (See IRB Policy, "Administrative Hold, Suspension, and Termination of IRB Approval).
3. Once notified of the expiration, the Investigator must immediately submit to the IRB Chair, a list of research subjects for whom expiration of the research would cause harm.
 - a. The full IRB Committee reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB determines that it is in their best interests.
4. Enrollment of new subjects cannot occur on or after the expiration of IRB approval.

VI. History Notes

This is a new policy. The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

VII. Signature Block with Effective Date



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Date