A. INITIAL AND CONTINUING REVIEW

Common OHRP Findings of Noncompliance
(1) Research Conducted without IRB Review
(2) Failure of IRB to Review HHS Grant Applications
(3) IRB Lacks Sufficient Information to Make Determinations Required for Approval of Research
(4) Inadequate IRB Review at Convened Meetings
(5) Inadequate Continuing Review
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Additional OHRP Guidance
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B. EXPEDITED REVIEW PROCEDURES

Common OHRP Findings of Noncompliance
(17) Inappropriate Use of Expedited Review Procedures for Initial or Continuing IRB Review

Additional OHRP Guidance
(20) Documentation for Initial and Continuing Expedited Review

A. INITIAL AND CONTINUING REVIEW

Common OHRP Findings of Noncompliance
(1) Research Conducted without IRB Review. HHS at 45 CFR 46.109(a) require that the IRB review and approve all non-exempt human subject research. OHRP finds that certain human subject research was conducted without IRB review.

(2) Failure of IRB to Review HHS Grant Applications. HHS regulations at 45 CFR 46.103(f) require that an institution with an approved assurance shall certify that each application for research has been reviewed and approved by the IRB.
(a) OHRP found numerous discrepancies between the title, date, and type of IRB approval reported on the face page of grant applications and the relevant documentation in IRB records.
(b) In reviewing IRB records, and in discussions with IRB members, IRB administrators, and research investigators, OHRP finds that the IRB consistently fails to review the grant application for proposed research.

(3) IRB Lacks Sufficient Information to Make Determinations Required for Approval of Research. OHRP is concerned that when reviewing protocol applications, the IRB often appears to lack sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111. For example, the IRB appears to review only minimal information regarding (a) subject recruitment and enrollment procedures; (b) the equitable selection of subjects; (c) provisions to protect
(4) Inadequate IRB Review at Convened Meetings. The minutes of IRB meetings, and our discussions with IRB members and administrators, indicate that little substantive review takes place at convened meetings. Most protocols undergoing [initial/continuing] review are neither individually presented nor discussed at a convened meeting by the IRB as a group. Furthermore, OHRP's inspection of available materials yielded scant evidence that IRB approval of research is consistently based on consideration of the determinations required under HHS regulations at 45 CFR 46.111. In specific, the IRB appears not to consider systematically and rigorously such issues as equitable selection of subjects and subject recruitment, privacy and confidentiality protections, and special protections required for vulnerable subjects.

(5) Inadequate Continuing Review. Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any modifications previously approved by the IRB (see OPRR Reports 95-01). Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

OHRP finds that continuing review of research by the IRB regularly failed to satisfy these requirements.

(7) Failure to Conduct Continuing Review at Least Once per Year. HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk and not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. Additionally, where the convened IRB specifies conditions for approval of a protocol that are to be verified as being satisfied by the IRB Chair or another IRB member designated by the Chair, the approval period must begin on the date the protocol was reviewed by the convened IRB, not on the date the IRB Chair or his or her designee verifies that IRB-specified conditions for approval have been satisfied.

OHRP found numerous instances in which {extensions beyond the expiration date were granted} OR {the IRB failed to conduct continuing review of research at least once per year}.

If the IRB does not re-approve the research by the specified expiration date, subject accrual should be suspended pending re-approval of the research by the IRB. (Enrollment of new subjects cannot
ordinarily occur after the expiration of IRB approval. Continuation of research interventions or interactions in already enrolled subjects should only continue when the IRB finds that it is in the best interests of individual subjects to do so. OHRP and IRBs must address on a case-by-case basis those rare instances where failure to enroll would seriously jeopardize the safety or well-being of an individual prospective subject.

**Additional OHRP Guidance**

(15) Primary Reviewer Systems. If the IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation (see (14) above). All other IRB members should at least receive and review a protocol summary (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111), the proposed informed consent document, and any advertising material. In addition, the complete documentation should be available to all members for review.

(16) Continuing Review for Follow up in Cooperative Protocol Research Program Protocols. Continuing IRB review is required as long as individually identifiable follow-up data are collected on subjects enrolled in HHS-supported Cooperative Protocol Research Program (CPRP) protocols. This remains the case even after a protocol has been closed at all sites and protocol-related treatment has been completed for all subjects.

**B. EXPEDITED REVIEW PROCEDURES**

**Common OHRP Findings of Noncompliance**

(17) Inappropriate Use of Expedited Review Procedures for Initial or Continuing IRB Review. HHS regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register at 63 FR 60364. OHRP finds that:

(a) The IRB inappropriately confounds the concepts of minimal risk and expedited review.
(b) Use of expedited review by the IRB has not been restricted to these categories. OHRP recommends that documentation for initial and continuing reviews that are conducted utilizing expedited review procedures include citation of the specific permissible categories (see 63 FR 60364) justifying the expedited review.

**Additional OHRP Guidance**

(20) Documentation for Initial and Continuing Expedited Review. OHRP recommends that documentation for initial and continuing reviews conducted utilizing expedited review procedures include the specific permissible categories (see 63 FR 60364) justifying the expedited review.

**H. MISCELLANEOUS OHRP GUIDANCE**

(68) Protocol Revisions - Incorporation Into Written Protocol. OHRP recommends that each revision to a research protocol be incorporated into the written protocol. This practice ensures that there is only one complete protocol with the revision dates noted on each revised page and the first page of the protocol itself. This procedure is consistent with the procedure used for revised and approved informed consent documents which then supersede the previous one.