

**Division of Compliance Oversight
Office for Human Research Protections (OHRP)
OHRP Compliance Oversight Activities: Determinations of Noncompliance
02/04/2009**

This document provides a list of determinations of noncompliance that OHRP has made in compliance oversight determination letters over the last several years.

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A. INITIAL AND CONTINUING REVIEW

- (1) [Research Conducted without IRB Review and/or Approval.](#)

In accordance with HHS regulations at 45 CFR 46.103(b) and 46.109(a), the IRB must review and approve all non-exempt human subject research covered by an assurance before the research can be conducted. We have determined that certain non-exempt human subjects research was conducted without IRB review and/or approval.

- (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 or proposal for research covered by the assurance has been reviewed and approved by an IRB designated under the institution's federalwide assurance. We have determined that the IRB consistently failed to review the grant application for proposed research for which the institution is the primary awardee. (see "IRB Review of Applications for HHS Support" <http://www.dhhs.gov/ohrp/humansubjects/guidance/aplrev.htm>)

- (3) [IRB Lacks Sufficient Information to Make Determinations Required for Approval of Research.](#)

We have determined that the IRB, when reviewing protocol applications, lacked sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111. For example, the IRB reviewed insufficient information regarding (a) risks to subjects and how they are minimized; (b) subject recruitment and enrollment procedures; (c) the equitable selection of subjects; (d) provisions to protect the privacy of subjects and maintain the confidentiality of data; and

(e) additional safeguards to protect the rights and welfare of subjects who are likely to be vulnerable.

(4) Inadequate IRB Review at Convened Meetings.

In accordance with HHS regulations at 45 CFR 46.108(b), review of proposed research must be conducted by the IRB at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas, except where expedited review is appropriate under HHS regulations at 45 CFR 46.110(b). We have determined that little substantive review took place at convened meetings. Protocols undergoing initial/continuing review and protocol amendments undergoing review were neither individually presented nor discussed at a convened meeting of the IRB. Furthermore, we have noted little evidence that IRB approval of research was consistently based on consideration of the determinations required under HHS regulations at 45 CFR 46.111. Specifically, the IRB appeared not to have considered systematically and rigorously such issues as risks to subjects and how they are minimized, equitable selection of subjects and subject recruitment, privacy and confidentiality protections, and additional safeguards for subjects likely to be vulnerable to coercion or undue influence.

(5) Members Present at Convened IRB Meetings Lacked the Expertise to Make Determinations Required for Approval of Research.

HHS regulations at 45 CFR 46.107(a) provide, among other things, that each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. In addition, the regulations provide that the IRB be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects and be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The convened IRB, when reviewing protocol applications, must have sufficient expertise among the members present at the meeting to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111. We have determined that the members of the IRB present at convened meetings did not have the background and expertise necessary to review the research being proposed.

(6) Approval of Research Not Approved by the IRB.

HHS regulations at 45 CFR 46.113 require that the IRB have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. In addition, HHS regulations at 45 CFR 46.112 provide that non-exempt human subjects research that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, such officials may not approve non-exempt human subjects research if it has not been approved by an IRB.

We have determined that the IRB voted to suspend research, and that an institutional official rescinded or delayed that suspension, in violation of HHS regulations at 45 CFR 46.113 and 112.

(7) Contingent Approval of Research with Substantive Changes and no Additional Review by the Convened IRB.

We have determined that the IRB frequently approved research contingent upon substantive modifications or clarifications that were directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111 without requiring additional review by the convened IRB. We have noted that when the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that the IRB needs in order to make the determinations required by the IRB under HHS regulations at 45 CFR 46.111, IRB approval of the proposed research must be deferred, pending subsequent review by the convened IRB of responsive material, unless the research is eligible for review under an expedited review procedure.

(8) IRB Meeting Convened without Quorum (No Nonscientist Present).

HHS regulations at 45 CFR 46.108(b) require that, except when an expedited review procedure is used, research be reviewed at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in a nonscientific area (hereinafter referred to as “nonscientist”). We have determined that the IRB failed to meet this requirement for certain IRB meetings. Thus, any actions taken at these meetings that required a quorum were not valid under the HHS regulations at 45 CFR part 46. We have emphasized that should the quorum fail during a meeting (e.g., those with conflicts being excused, early departures, absence of a nonscientist member), the IRB may not take further actions or votes that require a quorum unless the quorum is restored.

(9) IRB Meeting Convened without Quorum (Lack of a Majority).

HHS regulations at 45 CFR 46.108 require that, except when an expedited review procedure is used, the IRB review proposed research at convened meetings at which a majority of the members of the IRB are present. We have determined that the IRB failed to meet this requirement for certain IRB meetings. Thus, any actions taken at these meeting that required a quorum were not valid under the HHS regulations at 45 CFR part 46. We have emphasized that should the quorum fail during a meeting (e.g., those with conflicts being excused, early departures, absence of a nonscientist member), the IRB may not take further actions or votes that require a quorum unless the quorum can be restored.

(10) IRB Members with Conflicting Interest Participated in IRB Review of Research.

HHS regulations at 45 CFR 46.107(e) stipulate that no IRB member may participate in the IRB's initial or continuing review of a project in which the member has a conflicting interest, except to provide information requested by the IRB. We have determined that IRB members inappropriately participated in the initial and continuing review of protocols for which they had a conflicting interest, for example, by voting on protocols on which they were investigators.

(11) Inadequate Continuing Review.

Continuing review of research must be substantive and meaningful. HHS regulations describe at 45 CFR 46.111 (and at subparts B, C, and D of 45 CFR part 46 when applicable) the criteria that must be satisfied in order for the IRB to approve research. These criteria must be satisfied when the IRB conducts continuing review of research either at a convened meeting or under an expedited review procedure. These criteria include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and additional safeguards for subjects likely to be vulnerable to coercion or undue influence.

We have determined that continuing review of research by the IRB was not substantive and meaningful.

(12) 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, but 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 chairperson or another IRB member designated by the chairperson, continuing review must occur no later than one year after the date the protocol was reviewed by the convened IRB, not on the anniversary of the date the IRB chairperson or his or her designee verifies that IRB-specified conditions for approval have been satisfied.

We have determined that the IRB failed to conduct continuing review of research at least once per year and that in some cases the IRB has granted extensions beyond the expiration date of IRB approval.

(13) Continuing Review for Follow up of Subjects in Research Protocols.

HHS regulations at 45 CFR 46.109(e) state that an IRB shall conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year. HHS regulations at 45 CFR 46.102(f) define *human subject* as a living individual about whom an investigator (whether professional or student)

conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Even where (i) the research is permanently closed to the enrollment of new subjects; and (ii) all subjects have completed all research-related interventions, continuing review is required as long as the research remains active for long-term follow-up of subjects and continues to involve non-exempt human subjects research. Furthermore, continuing IRB review of research is required where the remaining research activities are limited to data analysis of individually identifiable private information (see 63 FR 60364-60367, category (8)). We have determined that continuing review did not occur in protocols involving follow-up activities.

B. EXPEDITED REVIEW PROCEDURES

(14) Inappropriate Use of Expedited Review Procedures for Initial or Continuing IRB Review.

HHS regulations at 45 CFR 46.108(b) require that the IRB review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas, except where expedited review is appropriate under HHS regulations at 45 CFR 46.110. HHS regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures for initial or continuing review to specific research categories published in the Federal Register at 63 FR 60364--60367 (see <http://www.dhhs.gov/ohrp/humansubjects/guidance/expedited98.htm>) when the research is determined to involve no more than minimal risk. We have determined that:

- (a) The IRB inappropriately applied expedited review to research that involved minimal risk but did not appear in the categories of research published in the Federal Register.
- (b) The IRB inappropriately applied expedited review to research that involved greater than minimal risk.

(15) Inappropriate Use of Expedited Review Procedures for Review of Protocol Changes.

HHS regulations at 45 CFR 46.108(b) require that the IRB review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas, except where expedited review is appropriate under HHS regulations at 45 CFR 46.110. HHS regulations at 45 CFR 46.110(b)(2) permit use of expedited procedures for review of minor changes in previously approved research during the period for which approval is authorized. We have determined that the IRB has employed expedited procedures to review changes that were more than minor.

(16) Failure to Advise IRB Members of Expedited Approvals.

HHS regulations at 45 CFR 46.110(c) require that all IRB members be advised of research proposals which have been approved under an expedited review procedure. We have determined that all IRB members were not advised of (a) research protocols approved at time of initial or continuing review under an expedited review procedure, or (b) minor changes in research protocols approved under an expedited review procedure.

(17) Expedited Review Conducted by Someone Other than an IRB Member.

HHS regulations at 45 CFR 46.110(b) state that under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among the members of the IRB. We have determined that an individual who was not a member of the IRB approved human subject research purportedly under an expedited review procedure, in violation of HHS regulations at 45 CFR 46.103(b), 45 CFR 46.109(a) and 45 CFR 46.110(b).

C. REPORTING OF UNANTICIPATED PROBLEMS, NONCOMPLIANCE, SUSPENSIONS, AND TERMINATIONS

(18) Failure to Report Unanticipated Problems, Noncompliance, Suspensions, and Terminations, to IRB, Institutional Officials, and OHRP.

We have determined that unanticipated problems involving risks to subjects or others *or* serious or continuing noncompliance *or* suspensions or terminations of IRB approval were not reported to appropriate institutional officials *or* the IRB *or* OHRP *or* the head of the sponsoring Federal department or agency as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5).

D. IRB REVIEW OF PROTOCOL CHANGES

(19) Changes to Research Initiated Without IRB Review and Approval.

HHS regulations at 45 CFR 46.103(b)(4)(iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. We have found no documentation that the IRB reviewed and approved protocol changes prior to initiation *or* we determine that certain protocol changes were initiated without IRB approval and/or approval, in circumstances where the changes were not necessary to eliminate apparent immediate hazards to the subjects.

(20) Inadequate IRB Review and/or Approval of Protocol Changes.

HHS regulations at 45 CFR 46.103(b)(4)(iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has

already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. We have determined that the IRB's procedures for reviewing protocol modifications was inadequate. In some cases, the IRB chairperson or designated IRB reviewer from among the IRB members approved such modifications in the absence of a complete description of the proposed changes.

We note that when reviewing proposed changes to research, the IRB must also receive sufficient information to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111 and, when applicable, under subparts B, C, and D of 45 CFR part 46, although we did not cite these regulatory provisions when making this determination in the past.

E. APPLICATION OF EXEMPTIONS

(21) Inappropriate Application of Exempt Categories of Research.

HHS regulations at 45 CFR 46.101(b) delineate six specific categories of research that are exempt from the requirements of 45 CFR part 46. We have determined that the institution applied an exemption to research activities that exceed these categories.

(22) Inappropriate Application of Exemption 4.

HHS regulations at 45 CFR 46.101(b)(4) exempt research that only involves the collection or study of existing data, documents, records, pathologic specimens, or diagnostic specimens provided specified conditions are met. We have noted that such materials must already exist at the time the research is proposed. We have determined instances where this exemption was applied to research involving data, documents, pathologic specimens, or diagnostic specimens that were not existing at the time the research was proposed.

(23) Inappropriate Application of Exemption 2 for Research Involving Children.

HHS regulations at 45 CFR 46.401(b) stipulate that the exemption at 45 CFR 46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by 45 CFR part 46, subpart D (Additional Protections for Children Involved as Subjects in Research), except for research involving observation of public behavior when the investigators do not participate in the activities being observed. We have determined that exemption 2 was inappropriately applied to survey and observational research involving children.

F. INFORMED CONSENT

(24) Failure of the Investigator to Obtain the Legally Effective Informed Consent of Subjects or of the IRB to Appropriately Waive the Requirements to Obtain Informed Consent.

HHS regulations at 45 CFR 45.116 state that no investigator may involve a human being as a subject in research covered by the regulations unless (a) the investigator has obtained the legally effective informed consent of the subjects or the subject's legally authorized representative, or (b) the IRB has waived the requirements to obtain informed consent in accordance with 45 CFR 46.116(c) or (d), or in accordance with the provisions for waiver of informed consent for research in emergent settings published in the Federal Register, Vol. 61, pp. 51531-51533. We have determined that the investigator initiated human subject research without obtaining legally effective informed consent of subjects and without the IRB appropriately waiving these requirements.

(25) Failure to Document Informed Consent or of the IRB to Appropriately Waive the Requirement to Document Informed Consent.

HHS regulations at 45 CFR 46.117(a) require that informed consent be documented by the use of a written consent form approved by the IRB and that is signed by the subject, or the subject's legally authorized representative, unless the IRB waives this requirement in accordance with 45 CFR 46.117(c). We have determined that informed consent was not documented by a written consent form signed by the subject(s) for this research and there was no IRB waiver of this requirement.

(26) Failure to Provide a Copy of the Informed Consent Document (ICD) to the Subject or the Subject's Legally Authorized Representative.

HHS regulations at 45 CFR 46.117(a) require that informed consent be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative unless the requirement for documentation of informed consent has been waived by the IRB in accordance with HHS regulations at 45 CFR 46.117(c). The regulations further require that a copy of the informed consent document shall be given to the person signing the form. We have determined that a copy of the informed consent document was not provided to the person signing the informed consent form.

(27) Inadequate ICD for Specific Research/Lack of Basic Elements.

HHS regulations at 45 CFR 46.116(a) require that when seeking informed consent specific information shall be provided to each subject unless the IRB approves a consent procedure which does not include, or which alters, some or all of the required basic elements of informed consent provided in accordance with 45 CFR 46.116 (c) or (d). We have determined that the informed consent documents reviewed and approved by the IRB failed to include and/or adequately address the following basic elements required by HHS regulations at 45 CFR 46.116(a):

- (a) Section 46.116(a)(1): (i) A statement that the study involves research; (ii) an explanation of the purposes of the research; (iii) the expected duration of the subject's participation; and (iv) a complete description of the

procedures to be followed, and identification of any procedures which are experimental.

- (b) Section 46.116(a)(2): A description of any reasonably foreseeable risks and discomforts.
- (c) Section 46.116(a)(3): A description of any benefits to the subject or others that may reasonably be expected from the research.
- (d) Section 46.116(a)(4): A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- (e) Section 46.116(a)(5): A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- (f) Section 46.116(a)(6): For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- (g) Section 46.116(a)(7): An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights (should include someone other than the investigator), and whom to contact in the event of a research-related injury to the subject.
- (h) Section 46.116(a)(8): A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Moreover, we found no documentation that the IRB approved a consent procedure which did not include, or which altered, some of the required basic elements of informed consent noted above in accordance with 45 CFR 46.116(c) or (d).

(28) Inadequate ICD for Specific Research/Lack of Additional Elements.

HHS regulations at 45 CFR 46.116(b) require that, when appropriate, additional elements of information shall be provided to subjects. We have determined that the following additional elements of informed consent should have been included in the informed consent documents under HHS regulations at 45 CFR 46.116(b):

- (a) Section 46.116(b)(1): A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
- (b) Section 46.116(b)(2): Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
- (c) Section 46.116(b)(3): Any additional costs to the subject that may result from participation in the research;
- (d) Section 46.116(b)(4): The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

- (e) Section 46.116(b)(5): A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
- (f) Section 46.116(b)(6): The approximate number of subjects involved in the study.

Moreover, we found no documentation that the IRB approved a consent procedure which did not include, or which altered, some of the required additional elements noted above in accordance with 45 CFR 46.116(c) or (d).

(29) ICD Language too Complex.

HHS regulations at 45 CFR 46.116 require that informed consent information be in language understandable to the subject or the subject's legally authorized representative. We have determined that the informed consent information provided to subjects would not be understandable to some subjects.

(30) Exculpatory Language in ICDs.

HHS regulations at 45 CFR 46.116 prohibit the inclusion of any exculpatory language in informed consent through which the subject is made to waive, or appear to waive, any of the subject's legal rights. We have determined certain language in the IRB-approved informed consent documents was exculpatory.

(31) Enrollment Procedures did not Minimize Possibility of Coercion or Undue Influence.

HHS regulations at 45 CFR 46.116 require that investigators seek the legally effective informed consent of subjects under circumstances that minimize the possibility of coercion or undue influence. We have determined that informed consent was not sought from prospective subjects under circumstances that minimized the possibility of coercion or undue influence.

G. IRB MEMBERSHIP, EXPERTISE, STAFF, SUPPORT, AND WORKLOAD

(32) Failure To Have An Unaffiliated IRB Member.

HHS regulations at 45 CFR 46.107(d) require that each IRB include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. We have determined that the IRB did not include any such member.

(33) Lack of Prisoner/Prisoner Representative for IRB Review of Research Involving Prisoners.

HHS regulations at 45 CFR 46.304 require that at least one member of an IRB that reviews research involving prisoners be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB only one IRB need satisfy this requirement. When the convened IRB reviews research involving prisoners (including initial review, continuing review, review of protocol modifications, and review of unanticipated problems involving risks to subjects or others), the prisoner or prisoner representative must be present as a voting member. We have determined that the IRB failed to meet this requirement when reviewing research projects involving prisoners.

(34) IRB Chairperson and Members Lack Sufficient Understanding of HHS Regulations.

HHS regulations at 45 CFR 46.107(a) provide, among other things, that the IRB shall be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects and shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. We have determined that the IRB chairperson and/or IRB members lacked a detailed understanding of the specific requirements of the HHS regulations for the protection of human subjects. As a result, IRB determinations sometimes deviated from these requirements.

(35) Designation of an Additional IRB under an FWA without Prior OHRP Approval.

HHS regulations at 45 CFR 46.103(b) state, in part, that assurances applicable to federally supported or conducted research shall include designation of one or more IRBs established in accordance with the requirements of the regulations, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.

Designation of additional IRBs under an FWA requires prior notification of and approval by OHRP. We have determined that the institution established an additional IRB that reviews research covered by its FWA without such approval.

(36) Inadequate IRB Resources.

HHS regulations at 45 CFR 46.103(b)(2) require that institutions provide meeting space and sufficient staff to support the IRB's review and recordkeeping duties. We have determined that the IRB lacked sufficient meeting space and/or staff to support the IRB's review and recordkeeping duties.

(37) Lack of IRB Knowledge of Local Research Context.

HHS regulations at 45 CFR 46.107(a) require, among other things, that the IRB be (a) sufficiently qualified through the diversity of the members, including consideration of

race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel; and (b) able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. Institutions have a responsibility to ensure that all IRBs designated under an OHRP-approved Assurance possess sufficient knowledge of the local research context to satisfy these requirements. We have determined that the IRB did not have the background and expertise to review the above-referenced research based on its failure to include members with sufficient understanding of the cultural conditions, including the social, economic, and political status, of the subject population.

We note that the IRB also must have sufficient background and expertise regarding the local research context in order to make the determinations required for approval of research as described within HHS regulations at 45 CFR 46.111 and applicable subparts, although we did not cite this regulatory provision when making this determination in the past.

(38) Lack of IRB Professional Competence to Review Specific Research Activities.

HHS regulations at 45 CFR 46.107(a) require, among other things, that the IRB possess the professional competence necessary to review specific research activities. We have determined that the IRB did not possess the professional competence necessary to review specific research activities.

We note that the IRB also must have sufficient professional competence in order to make the determinations required for approval of research under HHS regulations at 45 CFR 46.111, although we did not cite this regulatory provision when making this determination in the past. We also note that under HHS regulations at 45 CFR 46.107(f) an IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which are beyond or in addition to that available on the IRB and IRB's cited for this determination did not seek to invite individuals with competence in relevant special areas, although this was not noted when the determinations were originally made by OHRP.

H. IRB DOCUMENTATION, FINDINGS, AND PROCEDURES

(39) Lack of Appropriate Written IRB Procedures.

We have determined that the institution did not have written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

- (a) The procedures which the IRB will follow for conducting its initial review of research.
- (b) The procedures which the IRB will follow for conducting its continuing review of research.

- (c) The procedures which the IRB will follow for reporting its findings and actions to investigators and the institution.
- (d) The procedures which the IRB will follow for determining which projects require review more often than annually.
- (e) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.
- (f) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
- (g) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any department or agency head, and OHRP of: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

(40) Failure of an Institution Engaged In HHS-Conducted or –Supported Research to Hold an OHRP-Approved FWA.

HHS regulations at 45 CFR 46.103(a) require that each institution “engaged” in human subjects research provide OHRP with a satisfactory assurance to comply with the regulations, unless the research is exempt under 45 CFR 46.101(b). (Please see OHRP guidance at <http://www.dhhs.gov/ohrp/humansubjects/guidance/engage08.pdf>)

In general, an institution is considered *engaged* in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research [45 CFR 46.102(d),(f)].

We have determined that the institution was engaged in human subject research under a particular project and the institution was not covered by an OHRP-approved FWA for this research. If the project in question is ongoing, we have noted that involvement of the unassured institution in non-exempt human subject research activities under the specified HHS award must be suspended until OHRP approved an FWA, unless it is determined that it is in subjects’ best interest to continue.

(41) Inadequate IRB Records.

We have determined that IRB records fail to include all the documentation required by HHS regulations at 45 CFR 46.115(a).

(42) Inadequate IRB Minutes.

HHS regulations at 45 CFR 46.115(a)(2) require that minutes of IRB meetings be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. We have determined that minutes of IRB meetings failed to meet these requirements.

(43) Poorly Maintained IRB Files.

HHS regulations at 45 CFR 46.115(a) require that the institution prepare and maintain adequate documentation of IRB activities. We found that in numerous instances among the IRB files examined by OHRP, it was difficult to reconstruct a complete history of all IRB actions related to the review and approval of the protocol. In some instances, we could not determine what the IRB actually approved.

(44) Failure of IRB to Determine That Criteria for IRB Approval Are Satisfied.

HHS regulations at 45 CFR 46.111 delineate the criteria that must be satisfied in order for an IRB to approve research covered by the regulations. We have determined that for certain research the IRB failed to determine that the following requirements were satisfied:

- (a) Risks to subjects are minimized.
- (b) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- (c) Selection of subjects is equitable.
- (d) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.
- (e) Informed consent will be appropriately documented.
- (f) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- (g) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- (h) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of vulnerable subjects.

(45) Failure of IRB to Make Required Findings When Reviewing Research Involving Children.

HHS regulations at 45 CFR 46.404-407 require specific findings on the part of the IRB for approval of research involving children. We have determined that the IRB did not make the required findings when reviewing research involving children.

(46) Failure of IRB to Make Required Findings When Reviewing Research Involving Prisoners.

HHS regulations at 45 CFR 46.305-306 require specific findings on the part of the IRB for approval of research involving prisoners.

(a) We have determined that the IRB failed to make the required findings when reviewing such research.

(b) We have determined that the IRB approved research involving prisoners even though the research failed to satisfy subpart C criteria.

(47) Failure of IRB to Make and Document Required Findings for Waiver of Informed Consent.

HHS regulations at 45 CFR 46.116(c) and (d) require that the IRB find and document specific criteria when approving waiver or alteration of some or all of the required elements of informed consent. We have determined that the IRB failed to satisfy these requirements.

(48) Failure to Make Required Findings for IRB Waiver of a Signed Informed Consent Document.

HHS regulations at 45 CFR 46.117(c) requires specific findings on the part of the IRB for waiver of the requirements for the investigator to obtain a signed consent form from all subjects. We have determined that the IRB failed to make the required findings when approving such waivers.

(49) Inadequate Retention of IRB Records.

HHS regulations at 45 CFR 46.115(b) require that IRB records be retained for at least 3 years, and records relating to research which is conducted be retained for at least 3 years after completion of the research. All records must be accessible for inspection and copying by authorized representatives of HHS at reasonable times and in a reasonable manner. We have determined that the institution failed to retain IRB records OR records relating to research for at least 3 years after completion of the research at that study site.

(50) Failure to Notify Investigators/Institution of IRB Actions.

HHS regulations at 45 CFR 46.109(d) require that an IRB notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing. We have determined that the IRB did not notify investigators and the institution in writing of its decision to approve or disapprove proposed research or of modifications required to secure IRB approval of the research.

I. OTHER

(51) Failure of Signatory Official to Fulfill Obligations.

HHS regulations at 45 CFR 46.103(c) require that an institution's assurance of compliance with the regulations for the protection of human subjects shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by the regulations. We have determined that the Signatory Official failed to fulfill his or her obligations imposed by the HHS regulations for the protection of human subjects and the institution's FWA.

We note that HHS regulations at 45 CFR 46.103(a) require that each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in the regulations, although we did not cite this regulatory provision when making this determination in the past. Similarly, Public Law 99-158 Sec. 491(a) requires that the Secretary shall by regulation require that each entity which applies for a grant, contract, or cooperative agreement under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant, contract, or cooperative agreement assurances satisfactory to the Secretary.