

OHRP Determinations of Non-Compliance

The Office for Human Research Protections (OHRP) has made a number of different non-compliance oversight determinations at institutions over the last several years. The listing below is a subset of areas that have been violated at institutions, which fall under the responsibility of both the IRB and the Principal Investigator. Researchers should proactively review over these determinations to ensure their research protocols are being conducted in compliance with the federal regulations.

INITIAL AND CONTINUING REVIEW

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.

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.

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.

REPORTING OF UNANTICIPATED PROBLEMS, NONCOMPLIANCE, SUSPENSIONS, AND TERMINATIONS

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).

IRB REVIEW OF PROTOCOL CHANGES

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.

INFORMED CONSENT

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.

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.

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.

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).

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).

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.

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.

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.

Source of Information: <http://www.hhs.gov/ohrp/compliance/findings/>