

**TITLE 45
CODE OF FEDERAL REGULATIONS
PART 46**

**PROTECTION OF HUMAN SUBJECTS
Subpart A - Federal Policy for the
Protection of Human Subjects (Basic DHHS
Policy for Protection of Human Research Subjects)**

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§46.112 Review by institution.

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§46.113 Suspension or termination of IRB approval of research.

An IRB shall 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. Any suspension or termination or approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the Department or Agency head.

(Approved by the Office of Management and Budget under Control Number 9999-0020.)

§46.114 Cooperative research.

Cooperative research projects are those projects covered by this policy which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the Department or Agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of

another qualified IRB, or make similar arrangements for avoiding duplication of effort.

§46.115 IRB records.

(a) An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

- (1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
- (2) Minutes of IRB meetings which shall 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.
- (3) Records of continuing review activities.
- (4) Copies of all correspondence between the IRB and the investigators.
- (5) A list of IRB members in the same detail as described in §46.103(b)(3).
- (6) Written procedures for the IRB in the same detail as described in §46.103(b)(4) and §46.103(b)(5).
- (7) Statements of significant new findings provided to subjects, as required by §46.116(b)(5).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research which

is conducted shall be retained for at least 3 years after completion of the research. All records shall be accessible for inspection and copying by authorized representatives of the Department or Agency at reasonable times and in a reasonable manner. (Approved by the Office of Management and Budget under Control Number 9999-0020.)

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

- (1) a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
- (2) a description of any reasonably foreseeable risks or discomforts to the subject;
- (3) a description of any benefits to the subject or to others which may reasonably be expected from the research;
- (4) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- (5) a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- (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;
- (7) an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
- (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.

(b) additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

- (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;
- (2) anticipated circumstances under

which the subject's participation may be terminated by the investigator without regard to the subject's consent;

- (3) any additional costs to the subject that may result from participation in the research;
- (4) the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- (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; and
- (6) the approximate number of subjects involved in the study.

(c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

- (1) the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
- (2) the research could not practicably be carried out without the waiver or alteration.

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

- (1) the research involves no more than minimal risk to the subjects;
- (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) the research could not practicably be carried out without the waiver or alteration; and

(4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

(e) The informed consent requirements in this policy are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State, or local law.

(Approved by the Office of Management and Budget under Control Number 9999-0020.)

§46.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall 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. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said

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to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

- (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(Approved by the Office of Management and Budget under Control Number 9999-0020.)

§46.118 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon

completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101 (b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the Department or Agency.

§46.119 Research undertaken without the intention of involving human subjects.

In the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted, by the institution, to the Department or Agency, and final approval given to the proposed change by the Department or Agency.

§46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

(a) The Department or Agency head will evaluate all applications and proposals involving human subjects submitted to the Department or Agency through such officers and employees of the Department or Agency and such experts and consultants as the Department or Agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

(b) On the basis of this evaluation, the Department or Agency head may approve or disapprove the application or proposal, or enter into negotiations to develop an approvable one.

§46.121 [Reserved]

§46.122 Use of Federal funds.

Federal funds administered by a Department or Agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

§46.123 Early termination of research support: Evaluation of applications and proposals.

(a) The Department or Agency head may require that Department or Agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the Department or Agency head finds an institution has materially failed to comply with the terms of this policy.

(b) In making decisions about supporting or approving applications or proposals covered by this policy the Department or Agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the Department or Agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to Federal regulation).

§46.124 Conditions.

With respect to any research project or any class of research projects the Department or Agency head may impose additional conditions prior to or at the time of approval when in the judgment of the Department or Agency head additional conditions are necessary for the protection of human subjects.

- Tell prospective subjects they are subjects in research, not patients getting a new treatment.
- Describe a subject's rights and benefits.
- Describe how research information is shared. (Research privacy rights under HIPAA are different from treatment privacy rights).

The Language of Clinical Trials

The language of clinical trials contains similar, often interchangeable, words with different meanings. For example, are participants human subjects, patients, study volunteers, or study participants? Are participants enrolled in an experiment, study, research investigation, clinical research study, research project, clinical trial, research study, or medical research trial? Do participants receive study drugs, new drugs, study medications, investigational drugs, research (investigational products), investigational (experimental) agents, new investigational drugs, or new treatments? Are participants at risk for research-related injuries or research-related illness?

Will enrollment be enhanced by choosing certain words over others? For example, should the informed consent say "research subjects in an experiment who get an experimental drug and might experience a research-related injury" or "study volunteers in a clinical study who get a new drug and might experience a research-related illness?" Who decides which words to use? (*See Hochhauser, M. Who chooses the language of clinical trials? ARENA Newsletter, 2002, XV(3), 3-4.*)

Self Study Quiz - Answer Key

(See Pg. 9)

Answers:

1. b. true (Section 46.122)
2. a. true (Section 46.117 c)
3. b. an additional element (Section 46.116 b)
4. b. for, against, and abstained (Section 46.115 [2])
5. c. three (Section 46.115 b)
6. c. eight (Section 46.116)
7. b. research subject's rights and a research-related injury (Section 46.116 [7])
8. a. true (Section 46.116 [3])
9. b. false (Section 46.116 b)
10. a. one (Section 46.114)