



Redline of Common Rule NPRM

**Redline of
Unofficial Notice of Proposed Rulemaking
For the Common Rule (September 2, 2015)
Against
Health and Human Services Common Rule
At 45 C.F.R. Part 46, Subpart A (Current)**

This redline was prepared on September 3, 2015 by the Academic and Clinical Research Group (“ACRG”) of Verrill Dana, LLP. For more information, please feel free to contact one of the following members of the ACRG:

Kate Gallin Heffernan (Chair)
(617) 274-2858
kheffernan@verrilldana.com

Mark A. Borreliz
(617) 274-2845
mborreliz@verrilldana.com

Emily Chi Fogler
(617) 274-2619
efogler@verrilldana.com

Andrew P. Rusczek
(617) 274-2856
arusczek@verrilldana.com

Note: This redline is being provided for reference purposes only and should not be relied upon as an exact statement of either the Common Rule (at 45 C.F.R. Part 46, Subpart A) or the regulations proposed in the NPRM. This redline does not track formatting or citations, footnotes, or other notations in either the Common Rule (at 45 C.F.R. Part 46, Subpart A) or the NPRM. For more information on the regulatory provisions highlighted in this redline, consult either the applicable agency’s Common Rule or the NPRM.

PART ~~46~~—__ PROTECTION OF HUMAN SUBJECTS

<p style="text-align: center;">Key</p> <p><u>Added text</u></p> <p>Deleted text</p> <p><u>Text moved from here</u></p> <p><u>Text moved to here</u></p>

~~46.101~~ .101 To what does this policy apply?

~~46.102~~ .102 Definitions for purposes of this policy.

~~46.103~~ .103 Assuring compliance with this policy—research conducted or supported by any Federal ~~Department~~department or ~~Agency~~agency.

~~46.104–46.106~~ [~~Reserved~~]

.104 Exempt research.

.105 Protection of biospecimens and identifiable private information.

.106 [Reserved]

~~46.107~~ .107 IRB membership.

~~46.108~~ .108 IRB functions and operations.

~~46.109~~ .109 IRB review of research.

~~46.110~~ .110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

~~46.111~~ .111 Criteria for IRB approval of research.

~~46.112~~ .112 Review by institution.

~~46.113~~ .113 Suspension or termination of IRB approval of research.

~~46.114~~ .114 Cooperative research.

~~46.115~~ .115 IRB records.

~~46.116~~ .116 General requirements for informed consent.

~~46.117~~ .117 Documentation of informed consent.

~~46.118~~ .118 Applications and proposals lacking definite plans for involvement of human subjects.

~~46.119~~ .119 Research undertaken without the intention of involving human subjects.

~~46.120~~ .120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal ~~Department~~department or ~~Agency~~agency.

~~46.121~~ .121 [Reserved]

~~46.122~~ .122 Use of Federal funds.

~~46.123~~ .123 Early termination of research support: Evaluation of applications and proposals.

~~46.124~~ .124 Conditions.

§ ~~46.101~~ .101 To what does this policy apply?

(a) Except as provided in paragraph (b) of this section, ~~this policy applies to all~~ and as detailed in § .104, this policy applies to the research described in paragraphs (a)(1) and (2) of this section. The entities that must comply with this policy are institutions that are engaged in research described in paragraphs (a)(1) or (2) of this section, and institutional review boards (IRBs) reviewing research that is subject to this policy.

(1) All research involving human subjects conducted, supported, or otherwise subject to regulation by any ~~federal~~Federal department or agency ~~which~~that takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by ~~federal~~Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the ~~federal government~~Federal Government outside the United States.

~~(1) Research that is conducted or supported by a federal department or agency, whether or not it is regulated as defined in §46.102(e), must comply with all sections of this policy.~~

(2) All clinical trials as defined by this policy, irrespective of funding source, that meet all of the following conditions: (i) The clinical trials are conducted by an institution that receives support from a Federal department or agency for human subjects research that is not excluded from this policy under § .101(b)(2) and does not qualify for exemption in accordance with § .104; (ii) The clinical trials are not subject to regulation by the Food and Drug Administration; and (iii) The clinical trials are conducted at an institution located within the United States.

~~(2) Research that is neither conducted nor supported by a federal department or agency but is subject to regulation as defined in §46.102(e) must be reviewed and~~

~~approved, in compliance with §46.101, §46.102, and §46.107 through §46.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.~~

(b) The following categories of activities are excluded from this policy, and no procedural, recordkeeping, or other requirements of this policy apply to the activities other than the conditions specified for the relevant category or categories:

~~(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:-~~

~~(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.~~

~~(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.~~

(1) The following activities are excluded because they are deemed not to be research, as defined in § .102(l), for the purposes of this regulation:

(i) Data collection and analysis, including the use of biospecimens, for an institution's own internal operational monitoring and program improvement purposes, if the data collection and analysis is limited to the use of data or biospecimens originally collected for any purpose other than the currently proposed activity, or is obtained through oral or written communications with individuals (e.g., surveys or interviews).

(ii) Oral history, journalism, biography, and historical scholarship activities that focus directly on the specific individuals about whom the information is collected.

(iii) Collection and analysis of data, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(iv) Quality assurance or improvement activities involving the implementation of an accepted practice to improve the delivery or quality of care or services (including, but not limited to, education, training, and changing procedures related to care or services) if the purposes are limited to altering the utilization of the accepted practice and collecting data or biospecimens to evaluate the effects on the utilization of the practice. This exclusion does not cover the evaluation of an accepted practice itself.

(v) Public health surveillance activities, including the collection and testing of biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority and limited to those necessary to allow the public health authority to identify, monitor, assess, or investigate potential public health signals or the onset of a disease outbreak, including trends, or signals, and patterns in diseases, or a sudden increase in injuries from using a consumer product, or conditions of public health importance, from data, and including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health, including natural or man-made disasters.

(vi) Surveys, interviews, surveillance activities and related analyses, or the collection and use of biospecimens conducted by a defense, national security, or homeland security authority solely for authorized intelligence, homeland security, defense, or other national security purposes.

(2) The following activities are excluded because they are considered to be low-risk human subjects research, when already subject to independent controls without application of these regulatory requirements. These exclusions do not apply when the research includes the collection or analysis of biospecimens. All of the following exclusion categories apply to research subject to this policy and to research subject to the additional requirements of 45 CFR part 46, subparts B, C, and D, however, the exclusion at paragraph (b)(2)(i) of this section applies only to research subject to subpart D for research involving educational tests, or observations of public behavior when the investigator does not participate in the activities being observed.

~~(3) Research involving, not including interventions, that involves the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if: (i) The human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research-~~

~~and thereafter.~~ (including visual or auditory recording) uninfluenced by the investigators, if at least one of the following criteria is met:

(A) The information is recorded by the investigator in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or (C) The research will involve a collection of information subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.; research information will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note; and all of the information collected, used, or generated as part of the research will be maintained in a system or systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a.

(4ii) Research, involving the collection or study of ~~existing data, documents, records, pathological specimens, or diagnostic specimens, if these~~ information that has been or will be acquired solely for non-research activities or were acquired for research studies other than the proposed research study, when either of the following two criteria is met:

(A) These sources are publicly available, or ~~if the~~

(B) The information is recorded by the investigator in such a manner that human subjects cannot be identified, directly or through identifiers linked to the subjects, ~~the investigator does not contact the subjects, and the investigator will not re-identify subjects or otherwise conduct an analysis that could lead to creating identifiable private information.~~

(iii) Research conducted by a Federal department or agency using government-generated or government-collected information obtained for non-research purposes (including criminal history data), if the information originally involved a collection of information subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.; the information is maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note; and all of the information collected, used, or generated as part of the research is maintained in

a system or systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a.

(iv) Research as defined by this policy that involves only data collection and analysis involving the recipient's use of identifiable health information when such use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for the purpose of "public health activities" as described under 45 CFR 164.512(b).

(3) The following activities are excluded because they are considered to be low-risk human subjects research activities that do not meaningfully diminish subject autonomy. The following exclusion category applies to research subject to this policy and to research subject to the additional requirements of 45 CFR part 46, subparts B, C, or D.

(i) The secondary research use of a non-identified biospecimen that is designed only to generate information about an individual that already is known, including but not limited to the development and validation of certain tests and assays (such as research to develop a diagnostic test for a condition using specimens from individuals known to have the condition and those known not to have the condition), quality assurance and control activities, and proficiency testing.

(ii) [Reserved]

~~(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are 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.~~

~~(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.~~

(c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy, which judgment shall be exercised consistent with the ethical principles of the Belmont Report.

- (d) Department or agency heads may require ~~that~~additional protections for specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the Federal department or agency but not otherwise covered by this policy,~~comply with some or all of the requirements of this policy.~~ Advance public notice will be required when those additional requirements apply to entities outside of the Federal department or agency itself.
- (e) Compliance with this policy requires compliance with pertinent federal laws or regulations ~~which~~that provide additional protections for human subjects.
- (f) This policy does not affect any state or local laws or regulations ~~which~~that may otherwise be applicable and ~~which~~that provide additional protections for human subjects.
- (g) This policy does not affect any foreign laws or regulations ~~which~~that may otherwise be applicable and ~~which~~that provide additional protections to human subjects of research.
- (h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. ~~[An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.]~~ In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the ~~FEDERAL REGISTER~~Federal Register or will be otherwise published as provided in department or agency procedures.
- (i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy provided the alternative procedures to be followed are consistent with the principles of the Belmont Report. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Human Research Protections, Department of Health and Human Services (HHS), or any successor office, or to the equivalent office within the appropriate Federal department or agency, and shall also publish them in the ~~FEDERAL REGISTER~~Federal Register or in such other manner as provided in department or agency procedures. The waiver notice must include a statement that identifies the conditions under which the waiver will be applied and a justification as to why the waiver is appropriate for the research, including how the decision is consistent with the principles in Belmont Report. Each Federal department or agency conducting or supporting

the research must establish, on a publicly accessible federal website, a list of the research for which a waiver has been issued.

(j) Federal guidance on the requirements of this policy shall be issued only after consultation, for the purpose of harmonization (to the extent appropriate), with other Federal departments and agencies that have adopted this policy, unless such consultation is not feasible.

(k) Transition provisions—

(1) Research initiated prior to the compliance dates. Ongoing human subjects research in which human subjects (as defined by this policy) were involved prior to the compliance dates for the cited provisions need not comply with the additional requirements of this subpart at §§ .101(a)(2), .103(e), .104(c) through (f), .105, .108(a)(2), .109(f)(2), .111(a)(7) and (8), .114, .115(a)(10) and (11), .116, and .117 that became effective on [effective date of the final rule].

(2) Use of prior collections of biospecimens. Research involving the use of prior collections of biospecimens that meets both of the following criteria need not comply with the requirements of these regulations:

(i) The biospecimens were collected for either research or non-research purposes before the compliance date for the additional requirements of this subpart at § .102(e)(1)(iii), and (ii) Research use of the biospecimens occurs only after removal of any individually identifiable information associated with the biospecimens.

§ ~~46.102~~ .102 Definitions—for purposes of this policy.

(a) Certification means the official notification by the institution to the supporting Federal department or agency component, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

(b) Clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

(c) Department or agency head means the head of any ~~federal~~Federal department or agency, for example, the Secretary, HHS, and any other officer or employee of any Federal department or agency to whom the authority provided to the department or agency head by these regulations has been delegated.

~~(b) Institution means any public or private entity or agency (including federal, state, and other agencies).~~

~~(c) Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.~~

~~(d) Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.~~

(d) Federal department or agency refers to a Federal department or agency (the department or agency itself rather than its bureaus, offices or divisions) that takes appropriate administrative action to make this policy applicable to the research involving human subjects it conducts, supports, or otherwise regulates (e.g., HHS, the Department of Defense, or the Central Intelligence Agency).

~~(e) Research subject to regulation, and similar terms are intended to encompass those research activities for which a federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).~~

~~(f)~~

(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research ~~obtains (1)~~:

(i) ~~Data~~ Obtains data through intervention or interaction with the individual, ~~or (2) Identifiable~~ and uses, studies, or analyzes the data;

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information; or

(iii) Obtains, uses, studies, or analyzes biospecimens.

(2) Intervention includes both physical procedures by which data are gathered (for example, e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

(3) Interaction includes communication or interpersonal contact between investigator

and subject.

(4) Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information ~~which~~that has been provided for specific purposes by an individual and ~~which~~that the individual can reasonably expect will not be shared or made public (~~for example~~e.g., a medical record or clinically obtained biospecimen).

(5) ~~Private~~ Identifiable private information ~~must be~~is private information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) ~~in order for obtaining the information to constitute research involving human subjects.~~

(f) Institution means any public or private entity, or department or agency (including federal, state, and other agencies).

(g) IRB means an institutional review board established in accord with and for the purposes expressed in this policy.

(h) IRB approval means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(i) Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

(j) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The Secretary of HHS will maintain guidance that includes a list of activities considered to involve no more than minimal risk. This list will be re-evaluated no later than every 8 years based on recommendations from the Federal departments and agencies and the public.

~~(j) Certification means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.~~

(k) Public health authority (consistent with 45 CFR 164.501) means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with

such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

(l) Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

§ ~~46.103~~ .103 Assuring compliance with this policy—research conducted or supported by any Federal ~~Department~~department or ~~Agency~~agency.

(a) Each institution engaged in research ~~which~~that is covered by this policy ~~and which,~~
with the exception of research excluded from this policy under § .101(b) or eligible for exemption under § .104(d), and that is conducted or supported by a ~~federal~~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~~of this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections, HHS, or any successor office, and approved for federalwide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Human Research Protections, HHS, or any successor office. ~~(b)-~~
~~Departments~~Federal departments and agencies will conduct or support research covered by this policy only if the institution has provided an assurance ~~approved~~that it will comply with the requirements of this policy, as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB. ~~provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall at a minimum include:-~~

~~(1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department or agency supported~~

~~or regulated research and need not be applicable to any research exempted or waived under §46.101(b) or (i).~~

~~(2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.~~

~~(3) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with §46.103(a) of this policy, the existence of an HHS approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.~~

~~(4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) 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.~~

~~(5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.~~

(e) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.

~~(d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the~~

~~adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution. (e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one.~~

(c) The department or agency head may limit the period during which any ~~particular approved assurance or class of approved assurances~~ shall remain effective or otherwise condition or restrict ~~approval.~~ the assurance.

(d) Certification is required when the research is supported by a ~~federal~~ Federal department or agency and not otherwise ~~exempted or waived under §46.101 (b) or (i).~~ ~~An institution with an approved assurance excluded under § .101(b), waived under § .101(i), or exempted under § .104(d), (e), or (f)(2).~~ Institutions shall certify that each ~~application or~~ proposal for research covered by ~~the assurance and by §46.103 of this Policy~~ this § .103 has been reviewed and approved by the IRB. Such certification must be submitted ~~with the application or proposal or by such later date as may be~~ as prescribed by the Federal department or agency ~~to which the application or proposal is submitted~~ component supporting the research. Under no condition shall research covered by ~~§46.103 of the Policy be supported~~ this § .103 be initiated prior to receipt of the certification that the research has been reviewed and approved by the IRB. ~~Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.~~

(e) For non-exempt research involving human subjects covered by this policy that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall establish and follow procedures for documenting the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy (e.g., in a written agreement between the institution and the IRB, or by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution).

~~§§ 46.104–46.106 [Reserved]~~

§ .104 Exempt research.

(a) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the categories in paragraphs (d)

through (f) of this section are not subject to the requirements of this policy, other than those specified in the category.

(b) Use of the exemption categories for research subject to the requirements of subparts B, C, and D. Application of the exemption categories to research subject to the requirements of 45 CFR part 46, subparts B, C, and D, is as follows:

(1) Subpart B. Each of the exemptions at this § .104 may be applied to research conducted under subpart B if the conditions of the exemption are met.

(2) Subpart C. The exemptions at this § .104 do not apply to research conducted under subpart C, except for research aimed at a broader population that consists mostly of non- prisoners but that incidentally includes some number of prisoners.

(3) Subpart D. Only the exemptions at paragraphs (d)(1), (2), (4), (e)(2), and (f)(1) and (2) of this section may be applied to research conducted under subpart D if the conditions of the exemption are met.

(c) Federal departments and agencies shall develop a decision tool to assist in exemption determinations. Unless otherwise required by law, exemption determinations shall be made by an individual who is knowledgeable about the exemption categories and who has access to sufficient information to make an informed and reasonable determination, or by the investigator or another individual at the institution who enters accurate information about the proposed research into the decision tool, which will provide a determination as to whether the study is exempt. If the decision tool is used, further assessment or evaluation of the exemption determination is not required. An institution or, when appropriate, the IRB, must maintain records of exemption determinations made for research subject to the requirements of this policy for which the institution or IRB exercises oversight responsibility. These records must include, at a minimum, the name of the research study, the name of the investigator, and the exemption category applied to the research study. Maintenance of the completed decision tool shall be considered to fulfill this recordkeeping requirement.

(1) For studies exempted pursuant to paragraph (d)(2) of this section, the recordkeeping requirement will be deemed satisfied by the published list required at paragraph (d)(2)(i) of this section.

(2) [Reserved] .

(d) The following categories of exempt human subjects research generally involve a low-risk intervention with human subjects, must be recorded as required in paragraph (c) of this section, and do not require application of standards for information and biospecimen protection provided in § .105 or informed consent. Only paragraph (d)(2) of this section allows for the collection

and use of biospecimens:

(1) Research conducted in established or commonly accepted educational settings when it specifically involves normal educational practices. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods that are not likely to adversely impact students' opportunity to learn required educational content in that educational setting or the assessment of educators who provide instruction.

(2) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads, and that are designed to study, evaluate, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible federal website or in such other manner as the department or agency head may prescribe, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to or upon commencement of the research.

(ii) [Reserved]

(3)

(i) Research involving benign interventions in conjunction with the collection of data from an adult subject through verbal or written responses (including data entry) or video recording if the subject prospectively agrees to the intervention and data collection and at least one of the following criteria is met:

(A) The information obtained is recorded in such a manner that human subjects cannot be identified directly or through identifiers linked to the subjects; or

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation.

(ii) For the purpose of this provision, benign interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. If these criteria are met, such benign interventions might include research activities in which a subject is asked to read materials, review pictures or videos, play online games, solve puzzles, or perform cognitive tasks.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception as described in paragraph (d)(3)(iv) of this section.

(iv) For the purpose of this provision, authorized deception is prospective agreement by the subject to participate in research where the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Taste and food quality evaluation and consumer acceptance studies

(i) If wholesome foods without additives are consumed, or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

(e) The following categories of exempt human subjects research allow for the collection of sensitive information about human subjects, must not involve biospecimens, must be recorded as required in paragraph (c) of this section, and require application of standards for information and biospecimen protection provided in § .105:

(1) Research, not including interventions, involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording), if the information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects.

(2) Secondary research use of identifiable private information that has been or will be acquired for non-research purposes, if the following criteria are met:

(i) Prior notice has been given to the individuals to whom the identifiable

private information pertains that such information may be used in research; and

(ii) The identifiable private information is used only for purposes of the specific research for which the investigator or recipient entity requested access to the information.

(f) The following categories of exempt human subjects research involve biospecimens or identifiable private information, must be recorded as required in paragraph (c) of this section, require application of standards for information and biospecimen protection as described in § .105, and require informed consent and limited IRB review to the extent described in each category or otherwise required by law:

(1)

(i) Storage or maintenance for secondary research use of biospecimens or identifiable private information that have been or will be acquired for research studies other than for the proposed research study, or for non-research purposes, if the following criteria are met:

(A) Written consent for the storage, maintenance, and secondary research use of the information or biospecimens is obtained in accordance with § .116(c) and (d)(2), and the template published by the Secretary of HHS in accordance with § .116(d)(1) must be used. Oral consent, if obtained during the original data collection and in accordance with § .116(c) and (d)(3), would be satisfactory for the research use of identifiable private information initially acquired in accordance with activities excluded from this policy under § .101(b)(2)(i) or exempt from this policy in accordance with § .104(d)(3) or (4), or § .104(e)(1);

(B) The reviewing IRB makes the determinations required by § .111(a)(9).

(ii) [Reserved.]

(2)

(i) Research involving the use of biospecimens or identifiable private information that have been stored or maintained for secondary research use, if consent for the storage, maintenance, and secondary research use of the information and biospecimens was obtained as detailed in paragraph (f)(1)(i)(A) of this section.

(ii) If the investigator anticipates that individual research results will be provided to a research subject, the research may not be exempted under this provision and must be reviewed by the IRB and informed consent for the research must be obtained to the extent required by § .116(a) and (b).

§ .105 Protection of biospecimens and identifiable private information

(a) In General. Institutions and investigators conducting research that is subject to this policy, or that is exempt from this policy under § .104(e) or (f), involving the collection, storage, or use of biospecimens or identifiable private information, shall implement and maintain reasonable and appropriate safeguards as specified in paragraph (b) of this section to protect biospecimens or identifiable private information that they collect, obtain, receive, maintain, or transmit for research. The safeguards shall reasonably protect against anticipated threats or hazards to the security or integrity of the information or biospecimens, as well as reasonably protect the information and biospecimens from any intentional or unintentional use, release, or disclosure that is in violation of paragraph (c) of this section. IRB review of the safeguards required by this section is not required, except to the extent required by § .104(f)(1).

(b) Safeguards requirements. The Secretary of HHS shall establish and publish for public comment a list of specific measures that the institution or investigator may implement that will be deemed to satisfy the requirement for reasonable and appropriate safeguards. The list will be evaluated as needed, but at least every 8 years, and amended, as appropriate, after consultation with other Federal departments and agencies. The institutions and investigators identified in paragraph (a) of this section shall implement paragraph (a) of this section by choosing either to apply the safeguards identified by the Secretary as necessary to protect the security or integrity of and limit disclosure of biospecimens and electronic and non-electronic identifiable private information, or to apply safeguards that meet the standards in 45 CFR 164.308, 164.310, 164.312, and 45 CFR 164.530(c). For Federal departments and agencies that conduct research activities that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and the research will involve a collection of information subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq., these research activities automatically will be considered in compliance with the Secretary's reasonable and appropriate safeguards standards, unless or until any additional safeguards are identified by the Secretary of HHS.

(c) Limitations on use, release, and disclosure. Unless otherwise required by law, institutions and investigators shall use or release biospecimens or use or disclose identifiable private information collected or maintained for research only:

(1) For human subjects research regulated by this policy;

(2) For public health purposes;

(3) For any lawful purpose with the consent of the subject; or

(4) For other research purposes if the institution or investigator has obtained adequate assurances from the recipient that

(i) The recipient will implement and maintain the level of safeguards required by paragraph (b) of this section;

(ii) Except for research that qualifies for exclusion under § .101(b) or exemption under § .104 the releasing or disclosing institution or investigator shall obtain documentation from the recipient that the research has been approved under § .111 to the extent required before releasing biospecimens or disclosing identifiable private information; and

(iii) The recipient shall not further release the biospecimens or disclose identifiable private information except for human subjects research regulated by this policy, or for other purposes permitted by this paragraph. For the purposes of this requirement, an institution or investigator shall obtain adequate assurances through the use of a written agreement with the recipient that the recipient will abide by these conditions.

(d) The provisions of this section do not amend or repeal, and shall not be construed to amend or repeal, the requirements of 45 CFR parts 160 and 164 for the institutions or investigators, including Federal departments or agencies, to which these regulations are applicable pursuant to 45 CFR 160.102.

§ .106 [Reserved]

§ ~~46.107~~ .107 IRB membership.

(a) 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. The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of ~~the~~its 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 in safeguarding the rights and welfare of human subjects. ~~In addition to possessing the professional competence necessary to review specific research activities, the~~The

IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a ~~vulnerable~~ category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, ~~or handicapped~~physically or mentally disabled persons, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

~~(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.~~ (c) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

~~(d)~~ Each IRB shall 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.

~~(e)~~ No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

~~(f)~~ An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues ~~which~~that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

~~§ 46.108~~ § 46.108 IRB functions and operations.

(a) In order to fulfill the requirements of this policy each IRB shall:

~~(a) Follow written procedures in the same detail as described in §46.103(b)(4) and, to the extent required by, §46.103(b)(5).~~

(1) Have access to meeting space and sufficient staff to support the IRB's review and recordkeeping duties;

(2) Prepare and maintain a current list of the IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB

deliberations; and any employment or other relationship between each member and the institution, for example, full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant;

(3) Establish and follow written procedures for:

(i) Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;

(ii) Determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and

(iii) 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.

(4) Establish and follow written procedures for ensuring prompt reporting to the IRB; appropriate institutional officials; the department or agency head; and the Office for Human Research Protections, HHS, or any successor office, or the equivalent office within the appropriate Federal department or agency of

(i) Any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and

(ii) Any suspension or termination of IRB approval.

(b) Except when an expedited review procedure is used (~~see §46.110~~), as described in § .110, an IRB must 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. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§ ~~46.109~~ .109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy. ~~that do not qualify for exemption pursuant to § .104(d), (e), or (f)(2).~~

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §~~46.116~~; .116. The IRB may require that information, in addition to that specifically mentioned in §~~46.116~~; .116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent or may waive documentation in accordance with §~~46.117~~; .117.

(d) An IRB shall 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.

(e) An IRB shall conduct continuing review of research ~~covered by this policy~~requiring review by the convened IRB at intervals appropriate to the degree of risk, ~~but~~ not less than once per year, ~~and~~except as described in § .109(f).

(f)

(1) Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:

(i) Research eligible for expedited review in accordance with § .110;

(ii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition; or

(iii) Research reviewed by the IRB in accordance with the limited IRB review procedure described in § .111(a)(9).

(2) The IRB must receive confirmation on an annual basis that the research is still ongoing and that no changes have been made to the research that would require the IRB to conduct continuing review of the research.

(g) An IRB shall have authority to observe or have a third party observe the consent process and

the research.

§ ~~46.110~~ .110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Secretary, ~~of~~ of HHS, has established, and published as a Notice in the ~~FEDERAL REGISTER~~ Federal Register, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The ~~list will be amended~~ Secretary will evaluate the list at least every 8 years and amend it, as appropriate, after consultation with other federal departments and agencies, ~~through periodic republication by the Secretary, HHS, in the FEDERAL REGISTER and after publication in the Federal Register for public comment~~. A copy of the list is available from the Office for Human Research Protections, HHS, or any successor office.

(b)

(1) An IRB may use the expedited review procedure to review ~~either or both of the~~ following:

(i) Some or all of the research appearing on the list ~~and found by~~ unless the reviewer(s) ~~to involve no~~ determines that the study involves more than minimal risk;

(ii) Minor changes in previously approved research during the period ~~(of one-year or less)~~ for which approval is authorized; or

(iii) Research that is being reviewed to determine whether it qualifies for exemption in accordance with § .104(f)(1) in order to determine that the requirements of § .111(a)(9) are satisfied.

(2) 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 members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in § ~~46.108~~ .108(b).

(c) Each IRB ~~which~~ that uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals ~~which~~ that have been approved under the procedure.

(d) The department or agency head may restrict, suspend, terminate, or choose not to authorize an institution's or IRB's use of the expedited review procedure.

§ ~~46.111~~ .111 **Criteria for IRB approval of research.**

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized:

(i) By using procedures ~~which~~that are consistent with sound research design and ~~which~~that do not unnecessarily expose subjects to risk, and

(ii) ~~whenever~~Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) 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. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible ~~long-range~~long-range effects of applying knowledge gained in the research (~~for example e.g.~~, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research ~~involving~~that involves a category of subjects who are vulnerable ~~populations to~~coercion or undue influence, such as children, prisoners, pregnant women, physically or mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, ~~§ 46.116-~~ .116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by, ~~§ 46.117-~~ .117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, ~~in addition to the requirements in § .105, if the IRB determines that the standards for information and biospecimen protection in § .105~~

are not sufficient to protect the privacy of subjects and the confidentiality of data.

(8) If the investigator proposes a research plan for returning clinically relevant results to subjects, that the plan is appropriate.

(9) For purposes of conducting the limited IRB review as required by § .104(f)(1), the IRB need not make the determinations at paragraphs (a)(1) through (8) of this section, and shall determine that the following requirements are satisfied:

(i) The procedures for obtaining broad consent for storage, maintenance, and secondary research use of biospecimens or identifiable private information will be conducted in accordance with the requirements of the first paragraph in § .116.

(ii) If there will be a change for research purposes in the way the biospecimens or information are stored or maintained, that the privacy and information protection standards at § .105 are satisfied for the creation of any related storage database or repository.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, physically or mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§ ~~46.112~~ .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~~ .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 of 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.

§ ~~46.114~~ .114 Cooperative research.

(a) Cooperative research projects are those projects covered by this policy ~~which~~that 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.-

(b)

(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be selected by the Federal department or agency supporting or conducting the research or, if there is no funding agency, by the lead institution conducting the research.

(2) The following research is not subject to the requirements of this provision:

(i) Cooperative research for which more than single IRB review is required by law; or

(ii) Research for which the Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular study.

(c) For research not subject to paragraph (b) of this section~~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~~on the review of another ~~qualified~~ IRB, or make similar arrangements for avoiding duplication of effort.

§ ~~46.115~~ .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~~forms, 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, including the rationale for conducting continuing review of research that has progressed to the point that it involves only one or both of the following:

(i) Data analysis, including analysis of identifiable private information, or

(ii) Accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members in the same detail as described ~~is §46.103(b)(3)~~ in § .108(a)(2).

(6) Written procedures for the IRB in the same detail as described in ~~§46.103(b)~~ .108(a)(4) and ~~§46.103(b)(5)(4)~~.

(7) Statements of significant new findings provided to subjects, as required by ~~§46.116~~ .116(b)(5).

(8) The rationale for requiring continuing review for research that otherwise would not require continuing review as described in § .109(f)(1).

(9) The rationale for an expedited reviewer's determination that research appearing on the expedited review list described in § .110(b)(1)(i) is more than minimal risk.

(10) The written agreement between an institution and an organization operating an IRB specifying the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy, as described in § .103(e).

(11) Records relating to exemption determinations, as described in § .104(c).

(b) The records required by this policy shall be retained for at least 3 years, and records relating to research ~~which~~that is conducted shall be retained for at least 3 years after completion of the research. The institution or IRB may maintain the records in printed form, or electronically. All records shall be accessible for inspection and copying by authorized representatives of the Federal department or agency at reasonable times and in a reasonable manner.

(c) The institution or IRB retaining the records shall safeguard identifiable private information contained within these records in compliance with § .105.

~~§ 46.116~~ .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. The prospective subject or the representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information. The information must be presented in sufficient detail relating to the specific research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or representative's understanding of the reasons why one might or might not want to participate. In obtaining informed consent, the investigator must present first the information required by this section, before providing other information, if any, to the subject or the representative. Any informed consent form must include only the requirements of informed consent under this section, and appendices that include any other information provided to the subject or the representative. If an authorization required by 45 CFR parts 160 and 164 is combined with a consent form, the authorization elements required by 45 CFR 164.508 must be included in the consent form and not the appendices. 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), (e), or ~~(d)~~ of this section, in seeking informed consent the following information shall be provided to each subject or the representative:

- (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~~that 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~~that 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; and

(9) One of the following statements about any research that involves the collection of identifiable private information:

(i) A statement that identifiers might be removed from the data and the data that is not identifiable could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the representative, if this might be a possibility; or

(ii) A statement that the subject's data collected as part of the research, from which identifiers are removed, will not be used or distributed for future research studies.

(b) Additional elements of informed consent. ~~When~~Except as provided in paragraphs (c), (e), or (f) of this section, when appropriate, one or more of the following elements of information shall also be provided to each subject or the representative:

- (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~~that are currently unforeseeable;
- (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the representative'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~~that 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~~:-~~;

(7) A statement that the subject's biospecimens may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

(9) An option for the subject or the representative to consent, or refuse to consent, to investigators re-contacting the subject to seek additional information or biospecimens or to discuss participation in another research study.

(c)

(1) Elements of informed consent for broad consent to the storage, maintenance, and secondary research use of biospecimens or identifiable private information. If the subject or the representative will be asked to provide broad consent to the storage or maintenance of biospecimens or identifiable private information, collected for either research studies other than the proposed research or non-research purposes, and the secondary research use of this stored material, the information required in paragraphs (a)(2), (3), (5), and (7) and, if applicable, (b)(7) through (9) of this section, shall be provided to each subject, with the following additional information:

(i) A general description of the types of research that may be conducted with information and biospecimens and the information that is expected to be generated from the research, the types of information or biospecimens that might be used in research, and the types of institutions that might conduct research with the biospecimens or information;

(ii) A description of the scope of the informed consent must be provided, including:

(A) A clear description of the types of biospecimens or information that were or will be collected and the period of time during which biospecimen or information collection will occur. This may include all biospecimens and information from the subject's medical record or other records existing

at the institution at the time informed consent is sought; and

(B) For purposes of paragraph (c)(1)(ii)(A) of this section, the period of time during which biospecimen or information collection will occur cannot exceed 10 years from the date of consent. For research involving children as subjects, that time period cannot exceed 10 years after parental permission is obtained or until the child reaches the legal age for consent to the treatments or procedures involved in the research, whichever time period is shorter. The time limitations described do not apply to biospecimens or information that initially will be collected for research purposes.

(iii) A description of the period of time during which an investigator can continue to conduct research using the subject's biospecimens and information described in paragraph (c)(1)(ii)(A) of this section (e.g., a certain number of years, or indefinitely);

(iv) 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 that the subject may withdraw consent, if feasible, for research use or distribution of the subject's information or biospecimens at any time without penalty or loss of benefits to which the subject is otherwise entitled, and information about whom to contact in order for the subject to withdraw consent. The statement must make clear that information or biospecimens that already have been distributed for research use may not be retrieved;

(v) If applicable, a statement notifying the subject or the representative that the subject or the representative will not be informed of the details of any specific research studies that might be conducted, including the purposes of the research, that will use the subject's information and biospecimens;

(vi) If applicable, a statement notifying the subject or the representative of the expectation that the subject's information and biospecimens are likely to be used by multiple investigators and institutions and shared broadly for many types of research studies in the future, and this information and the biospecimens might be identifiable when shared;

(vii) The names of the institution or set of institutions at which the subject's biospecimens or information were or will be collected, to the extent possible (in recognition that institutions might change names or cease to exist); and

(viii) If relevant, an option for an adult subject or the representative to consent, or

refuse to consent, to the inclusion of the subject's data, with removal of the identifiers listed in 45 CFR 164.514(b)(2)(i)(A) through (Q), in a database that is publicly and openly accessible to anyone. This option must be prominently noted, and must include a description of risks of public access to the data.

(2) [Reserved]

(d)

(1) The Secretary of HHS will establish, and publish in the Federal Register for public comment, templates for consent that will contain all of the required elements of informed consent under paragraph (c) of this section. IRB review of the broad secondary use informed consent form obtained in accordance with paragraph (c) of this section is required unless the consent is obtained using only this template, without any changes.

(2) If § .104(f)(1) requires written consent, the consent for research use of biospecimens or identifiable private information must be documented by the use of a written consent form signed by the subject or the representative. The template for consent for research use established by the Secretary may serve as the written consent form. A copy shall be given to the person signing the form.

(3) If § .104(f)(1) allows for oral consent, a subject's or the representative's oral consent for research use of identifiable private information must be documented such that the consent is associated with the subject's identifiable private information. If this requirement is met through the use of written documentation, the subject or the representative is not required to sign the documentation.

(4) If the subject or the representative declines to consent to the research use of biospecimens or identifiable private information, this must be documented appropriately.

(e)

(1) Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials. An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above, or waive the above requirement to obtain informed consent, provided the IRB finds and documents that:

~~(e) 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~~A) Public benefit ~~of~~for service programs;

(~~ii~~B) ~~procedures~~Procedures for obtaining benefits or services under those programs;

(~~iii~~C) ~~possible~~Possible changes in or alternatives to those programs or procedures; or

(~~iv~~D) ~~possible~~Possible changes in methods or levels of payment for benefits or services under those programs; and

(~~2~~ii) The research could not practicably be carried out without the waiver or alteration.

(~~4~~2) Additional criteria for waiver or alteration of consent for biospecimens. For research involving the use of biospecimens, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above, or waive the above requirements to obtain informed consent, provided the IRB finds and documents the criteria in paragraph (e)(1) of this section, and the following additional criteria:

(i) There are compelling scientific reasons to conduct the research; and

(ii) The research could not be conducted with other biospecimens for which informed consent was obtained or could be obtained.

(3) If an individual was asked to consent to the storage or maintenance for secondary research use of biospecimens or identifiable private information in accordance with the requirements of this section at paragraph (c) of this section, and refused to consent, an IRB cannot waive consent for either the storage or maintenance for secondary research use, or for the secondary research use, of those biospecimens or information.

(f)

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

~~(4)~~ The research involves no more than minimal risk to the subjects;

~~(2i) The research could not practicably be carried out without the requested waiver or alteration;~~

~~(iii) If the research involves accessing or using identifiable biospecimens or identifiable information, the research could not practicably be carried out without accessing or using identifiers;~~

~~(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and~~

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

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

(2) Additional criteria for waiver or alteration of consent for research involving biospecimens. For research involving the use of biospecimens, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above, or waive the above requirements to obtain informed consent, provided the IRB finds and documents the criteria in paragraph (f)(1) of this section, and the following additional criteria:

(i) There are compelling scientific reasons for the research use of the biospecimens; and

(ii) The research could not be conducted with other biospecimens for which informed consent was obtained or could be obtained.

(3) If an individual was asked to consent to the storage or maintenance for secondary research use of biospecimens or identifiable private information, in accordance with the requirements of paragraph (c) of this section, and refused to consent, an IRB cannot waive consent for either the storage or maintenance for secondary research use, or for the secondary research use, of those biospecimens or information.

(g) An IRB may approve a research proposal in which investigators obtain, through oral or written communication or by accessing records, identifiable private information without individuals' informed consent for the purpose of screening, recruiting, or determining the eligibility of prospective human subjects of research, provided that the research proposal includes an assurance that the investigator will implement standards for protecting the

information obtained, in accordance with and to the extent required by § .105.

(h)

(1) A copy of the final version of the informed consent form for each clinical trial conducted or supported by a Federal department or agency must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available federal web site that will be established as a repository for such informed consent forms . The informed consent form must be posted in such form and manner as the department or agency head may prescribe, which will include at a minimum posting, in addition to the informed consent form, the name of the clinical trial and information about whom to contact for additional details about the clinical trial.

(2) The informed consent form must be posted on the federal website within 60 days after the trial is closed to recruitment.

(e) The informed consent requirements in this policy are not intended to preempt any applicable ~~federal~~Federal, state, or local laws ~~which~~that 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.

~~§ 46.117~~ .117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, and except for research for which consent is obtained in accordance with § .116(c), informed consent shall be documented by the use of a written informed 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 informed consent form.

(b) Except as provided in paragraph (c) of this section, the informed 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~~informed consent form that includes a form containing only the information required by § .116, and appendices that include any other information. The investigator shall give either the subject or the subject's legally authorized representative adequate opportunity to read ~~the informed consent form~~ before

it is signed; ~~or alternatively, this form may be read to the subject or the subject's legally authorized representative.~~

(2) A short form written informed consent document form stating that the elements of informed consent required by § ~~46.116~~ .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, and that the information required by § .116 was presented first to the subject, before other information, if any, was provided. The~~ IRB shall approve a written summary of what is to be said to the subject or the representative. When this method is used, there shall be a witness to the oral presentation. 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)

(1) An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds ~~either:~~ any of the following:

~~(1)~~ (i) That the only record linking the subject and the research would be the informed consent document form 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)~~ (ii) 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; ~~or~~

(iii) If the subjects are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. Documentation must include a description as to why signing forms is not the norm for the distinct cultural group or community.

(2) 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.

(3) This waiver does not apply to research for which consent is required to be documented in accordance with § .116(d)(2), (3), or (4).

(4) Documentation of informed consent may not be waived under paragraphs (c)(1)(i) or (iii) of this section for research subject to regulation by the Food and Drug Administration unless otherwise authorized by 21 CFR 56.109(c)(1).

§ 46.118 .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 Federal 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~~Except for research ~~exempted or excluded under § .101(b),~~ waived under ~~§ 46.101 (b) or (i)~~ .101(i), or exempted under § .104(d), (e), or (f)(2), 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 Federal department or agency component supporting the research.

§ 46.119 .119 Research undertaken without the intention of involving human subjects.

~~In~~Except for research excluded under § .101(b), waived under § .101(i), or exempted under § .104(d), (e), or (f)(2), 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 Federal department or agency component supporting the research, and final approval given to the proposed change by the Federal department or agency component.

§ 46.120 .120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal ~~Department~~department or ~~Agency~~agency.

(a) The department or agency head will evaluate all applications and proposals involving human subjects submitted to the Federal department or agency through such officers and employees of the Federal 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~~ .121 [Reserved]

§ ~~46.122~~ .122 Use of Federal funds.

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

§ ~~46.123~~ .123 Early termination of research support: Evaluation of applications and proposals.

(a) The department or agency head may require that Federal 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~~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~~ .124 Conditions.

With respect to any research project or any class of research projects the department or agency head of either the conducting or the supporting Federal department or agency 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.