

Summary of Revisions to Common Rule 45 CFR 46

As of **January 21, 2019** the **Federal Regulations** for the protection of human subjects has been revised. The federal Office of Human Research Protections (OHRP) has published the changes and the changes are referred to as the "Revised Common Rule" or the "Final Rule."

These changes will only impact new protocols submitted on and after January 21, 2019 or some studies that have not yet been reviewed and approved.

IMPORTANT CHANGES

Exempt Categories

Exempt Category -1 (REVISED)

Research, conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. 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.

Exempt Category -2 (REVISED)

Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

1. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
2. 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
3. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §11.111(a)(7).

Exempt Category -3 (NEW)

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

- (A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, 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 information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB

Benign behavioral interventions are defined as 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. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

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 through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research

Exempt Category –4 (REVISED)

Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

1. The identifiable private information or identifiable biospecimens are publicly available;
2. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

•*The major change here is that the specimens or information do not have to be existing at the time of the IRB application.*

3. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that 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 "public health activities and purposes" as described under 45 CFR 164.512(b); or
4. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities.

Exempt Category -5 (REVISED)

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 (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, 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. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, 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 commencing the research involving human subjects.

Exempt Category -6 (UNCHANGED)

Taste and food quality evaluation and consumer acceptance studies:

1. If wholesome foods without additives are consumed, or
2. 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.

Exempt Category -7 (NEW)

Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes determinations required by §11.111(a)(8).

Exempt Category -8 (NEW)

Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

1. Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §11.116(a)(1) through (4), (a)(6), and (d);
2. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §11.117;
3. An IRB conducts a limited IRB review and makes the determination required by §11.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and
4. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

Informed Consent

The Revised Common Rule requires changes to the structure and content of informed consent documents. (45 CFR 46.116 and 117)

- Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the consent form must be organized and presented in a way that facilitates comprehension.
- Informed consent as a whole must present information in sufficient detail relating to the 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 legally authorized representative's understanding of the reasons why one might or might not want to participate.

- Consent form must disclose any plans to conduct future research using information and/or biospecimens collected during the research.
- If applicable, consent form must disclose whether: a) subjects will share in commercial profit; b) clinically relevant research results will be returned; and c) research will or might include whole genome sequencing.
- Must be in language understandable to the subject of the legally authorized representative.

There have also been changes to the method of acceptable way of obtaining consent from participants and criteria for approval.

- Electronic consent is allowed, and a written copy must be provided to participants.
- Changes in the waiver and alteration criteria for consent.
- If applicable, must post copy of IRB-approved version of the consent form that was used for enrollment purposes for each clinical trial conducted or supported by a federal department or agency. Acceptable sites are Clinical Trials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

Nine basic elements of informed consent.

(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 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 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;

(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 or identifiable biospecimens:

(A) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens 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 legally authorized representative, if this might be a possibility; or

(B) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

Additional elements of informed consent.

One or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized 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) 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 legally authorized 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 that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects involved in the study;

(7) A statement that the subject's biospecimens (even if identifiers are removed) 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) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (*i.e.*, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Definitions

The Revised Common Rule contains updated definitions as well as newly defined terms.

Revised Existing terms

Human subject - Human subjects means a living individual about whom an investigator (whether professional or student) conducting research: obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Research - Now deems what's NOT research:

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities, including the collection and testing information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigating purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Vulnerable populations - the final rule no longer includes pregnant women or “handicapped” or physically disabled individuals as examples of populations that are potentially vulnerable to coercion or undue influence. The final rule uses the term “individuals with impaired decision making ability” to replace the term “mentally disabled persons.”

Legally Authorized Representative - Legally Authorized Representative means an individual or 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. If there are no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

New Terms Added:

Identifiable biospecimen - a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Public Health Authority - 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.

Written or in Writing - refers to writing on a tangible medium (e.g., paper) or in an electronic format.

Clinical Trial - 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.

Broad Consent is a new type of consent as an alternative to regular informed consent specifically for the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens. Use of broad consent is tied to the new exempt research categories 7 & 8.

Limited IRB Review is tied to exempt categories 2, 3, 7 & 8. Under exempt categories 2,3 & 8, limited IRB review requires that the IRB determines that the criteria for approval at 111(a)(7) is satisfied ; when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Under exempt category 7, limited IRB review also requires that the IRB determines that the proposed secondary research is within the scope of the broad consent and the requirements at .111(a)(8) are satisfied.

For more information:

View: <https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule>

View: <https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html#transition-provision>