Federal Regulations Regarding Human Subjects Research and Exempt Status

Relevant Definitions

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101(b)

§46.102 Definitions.

(a) *Department or agency head* means the head of any federal department or agency and any other officer or employee of any department or agency to whom authority 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.

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

(1) Data through intervention or interaction with the individual, or

(2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. *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 has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be 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.

(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) *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.

(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.

Information Regarding Exempt Status

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

§46.101 To what does this policy apply?

(a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by 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 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, must comply with all sections of this policy.

(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) 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.

(3) Research involving 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.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

(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.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported, or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

(e) Compliance with this policy requires compliance with pertinent federal laws or regulations which provide additional protections for human subjects.

(f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.

(g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which 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 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 or research activities otherwise covered by this policy. 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, and shall also publish them in the FEDERAL REGISTER or in such other manner as provided in department or agency procedures.[1]

1 Institutions with HHS-approved assurances on file will abide by provisions of Title 45 CFR part 46 subparts A-D. Some of the other departments and agencies have incorporated all provisions of Title 45 CFR part 46 into their policies and procedures as well. However, the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners, subpart C. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Guidance From Federal Government

http://www.hhs.gov/ohrp/policy/hsdc95-02.html

The purpose of this letter is to assist Institutional Officials and Institutional Review Board (IRB) Chairs in interpreting the term "exempt" research and identifying research for which "expedited review" is appropriate.

Research activities involving human subjects that are **exempt** from IRB review are identified in 45CFR 46.101(b)(1)-(6). (Institutions and IRBs may not create new categories of exempt researchunder 45 CFR Part 46.) Institutions should have a clear policy in place on who shall determinewhat research is exempt under .46.101(b). Those persons who have authority to make adetermination of what research is exempt are expected to be well-acquainted with interpretation of the regulations and the exemptions. In addition, the institution should be prepared to reinforce and review, as necessary, the method of determining what is exempt. OPRR advises that investigators should not have the authority to make an independent determination that research involving human subjects is exempt and should be cautioned to check with the IRB or other designated authorities concerning the status of proposed research or changes in ongoing research.

Institutions may elect to review all research under the auspices of the institution even if the research qualifies for exemption under .46.101(b). An institution with a Multiple Project Assurance (MPA) or Cooperative Project Assurance (CPA) should indicate in its Assurance if and how exempt research is reviewed. It is incumbent on the institution to advise investigators and others involved in the conduct and administration of research involving human subjects of the institutional policies for reviewing exempt research.

Exempt Research Determination - FAQs:

http://answers.hhs.gov/ohrp/categories/1564

Who may determine that research is exempt?

The regulations do not specify who at an institution may determine that research is exempt under 45 CFR 46.101(b)**.** However, OHRP recommends that, because of the potential for conflict of interest, investigators not be given the authority to make an independent determination that human subjects

research is exempt. (For more on this issue, see also Must there be review by someone other than the investigator before a research study is determined to be exempt?)**.**Institutions should implement exemption policies that most effectively address the local setting and programs of research. OHRP recognizes that this may result in a variety of configurations of exemption authority, any of which are acceptable assuming compliance with applicable regulations.

In developing policies and procedures addressing exemption, OHRP recommends that institutions consider the following:

- Persons making an exemption determination should have access to sufficient information to make a correct determination. Evaluation tools and resources may take a variety of forms, including but not restricted to: checklists, Standard Operating Procedures, or specialized training for individuals authorized by the institution to make an exemption determination.
- When an exemption determination is made, the specific exemption category or categories should be included in the record and this information should be available for oversight and audit purposes.
- Institutional policies and procedures should identify clearly who is responsible for making exemption decisions. This may be done in a variety of ways, including delegation by name, role, or position.
- Institutions should make policy and procedure information addressing exemption determination readily accessible to investigators and others involved in the conduct and administration of human subjects research.
- Regarding the possibility of exemption determinations being made without review by someone other than the investigator, please also see "Must there be review by someone other than the investigator before a research study is determined to be exempt?"

OHRP notes that the HHS retains final authority as to whether a particular human subjects research study conducted or supported by HHS is exempt from the HHS regulations (45 CFR 46.101(c))**.**

Must there be review by someone other than the investigator before a research study is determined to be exempt?

No, the regulations do not require that someone other than the investigator be involved in making a determination that a research study is exempt. What they do require is that there be accurate determinations so that non-exempt research ends up being reviewed by an IRB. Because of the potential for conflict of interest in this situation, OHRP's long-standing recommendation is that investigators not be given the authority to make an independent determination that human subjects research is exempt.

OHRP recognizes that some institutions will wish to take advantage of the regulatory flexibility so that exemption determinations can be made in a manner that minimally delays research, while at the same time not diminishing human subject protections. While an institutional policy that allowed investigators to make their own exemption determinations, without additional protections, would likely risk inaccurate determinations, institutions may be able to craft policies that build in protections which lead to accurate determinations by appropriately dealing with investigator conflicts of interest and lack of detailed knowledge of the regulations.

For example, an institution might craft a checklist for certain exemption categories, with questions that are easily answered "yes" or "no" by an investigator, with certain answers leading to a clear conclusion that the study is exempt. The institution might allow a researcher to immediately begin a study after having completed such a checklist and filed it, together with accompanying documents, with an appropriate institutional office, without waiting for or requiring any prior review of that filing. Similarly, a web-based form might be created that served the same purpose, allowing the researcher to begin the research immediately after submitting the required information using the web form. In both instances, the key issue would be whether these procedures lead to correct determinations that studies are exempt.

OHRP notes that the HHS retains final authority as to whether a particular human subjects research study conducted or supported by HHS is exempt from the HHS regulations (45 CFR 46.101(c)).