Exempt Human Subjects Research

Content Applies To
Mayo Clinic Human Research Protection Program
Research for which the Mayo Clinic is the IRB of Record

Purpose
The purpose of this document is to describe research activities involving human subjects that meet exemption criteria under 45 CFR 46.101 and 21 CFR 56.104.

Key Terms
**Exempt Research**: Research that qualifies for exemption from the requirements of federal regulations 45 CFR 46.101 or 21 CFR 56.104, including continuing review by the Institutional Review Board (IRB), and that meets the criteria within one or more of the six exempt categories designated in the federal regulations (45 CFR 46.101(b)).

**Human research subject**: A living individual about whom an investigator conducting research obtains data through intervention or interaction with an individual or with his/her identifiable private information, or an individual who is or becomes a subject in research, either as a recipient of the test article or as a control.

**Interaction**: Includes communication or interpersonal contact with a subject or their private identifiable information.

**Intervention**: 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.

**Research**: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Policy
It is the policy of the Mayo Clinic Office for Human Research Protection, Institutional Review Board (IRB), that all research activities under its jurisdiction involving human subjects be reviewed to determine whether the research meets one or more exemption categories, as defined by Federal regulations.

Exempt research activities are subject to the same human subject protections and ethical standards as outlined in the Belmont Report. Exempt research activities offer no more than minimal risk to participants, selection of participants is equitable, and adequate provisions are in place to maintain the privacy interests of participants. If there is recording of identifiable information, there are adequate provisions to maintain confidentiality of the data. If there are interactions with participants, the IRB will determine whether there should be a consent process that will disclose such information as the activity involves research, a description of the procedures, that participation is voluntary, and the name and contact information for the researcher.
Only the IRB may determine which activities qualify for exempt status. Investigators do not have the authority to make an independent determination that research involving human subjects is exempt and must contact the IRB concerning the status of proposed research or changes in ongoing research.

Determination of exempt status is generally performed by a designated IRB Specialist with demonstrated knowledge (of at least one year) of the application of research ethics in human subject protections. IRB Chairs, designated IRB members, Directors, and Administrators will review requests of exemption submitted by investigators, when applicable.

IRB review, action taken by the reviewer and the permissible exempt category citation(s), if applicable, are documented in IRBe.

When a research project has been determined by the IRB to be exempt from further IRB review, continuing review is not required.

**Exemption Status and Research Project Modifications**

Certain project modifications may disqualify the research from exempt status. Therefore, any proposed modification to an exempt study must be submitted to the IRB for review and approval prior to implementation.

**Investigator Responsibilities**

The investigator will make a preliminary assessment that a proposal is eligible for exemption based on the regulatory criteria and submit an application for IRB review.

The investigator will not begin the project until the exempt status is confirmed by the IRB.

**Criteria for Exemption**

Under 45 CFR 46.101 (b) (Department of Health and Human Services (DHHS)) the IRB may determine a research activity to be exempt where the only involvement of human subjects will be in one or more of the following six categories:

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 (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.

- The program under study delivers a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).
- The research is conducted pursuant to specific federal statutory authority.
- There is no statutory requirement that an IRB review the research.
- The research does not involve significant invasions or intrusions upon the privacy of subjects.

(6) Taste and food quality evaluation and consumer acceptance studies, if:
   (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.
FDA Exemption Criteria
Under 21 CFR 56.104 (Food and Drug Administration), the following categories of clinical investigations are exempt:

(a) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets FDA requirements in effect before July 27, 1981.

(b) Any investigation which commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

(c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

(d) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed, or 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 and Safety Inspection Service of the U.S. Department of Agriculture.

Research Involving Prisoners
These exemptions do not apply to research involving prisoners.

Research Involving Children
1. The exemptions specified in the above DHHS 45 CFR 46.101(b) exemption categories (1), (3), (4), (5), and (6) apply to research involving children.

2. The exemption specified in the above DHHS 45 CFR 46.101(b) exemption category (2) only applies to research involving observation of public behavior when the investigator does not participate in the activities being observed.

3. The exemption does not apply where the research involves survey or interview procedures or any direct interaction with the subjects being observed.

Related Documents
Exempt Human Subjects Research - IRB Review Instruction

References
45 CFR 46.101
21 CFR 56.104 Exemptions from IRB Criteria
OHRP Guidances:
Exempt Research and Research That May Undergo Expedited Review
Exemption for Research and Demonstration Projects on Public Benefit and Service Programs

Guidance on Research Involving Coded Private Information or Biological Specimens

**Effective Date**

May 21, 2014