

 JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH	Human Research Protection Program Policies & Procedures	
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Title: Review of New Applications	Date Effective April 5, 2005	Supercedes P&P dated November 5, 2004

BACKGROUND

All applications for new research projects that involve human subjects must be reviewed and approved by CHR before contact with human subjects may begin. Similarly, CHR must review and re-approve all ongoing research at least annually and all requests to amend the research plan before amendments are implemented.

Research Not Greater than Minimal Risk

The type of review required depends upon the level and type of risk involved. Studies that involve *no greater than minimal risk* may be classified either as *exempt* from Federal regulations or as requiring *expedited review*, depending on the details of the study. OHRP defines minimal risk as meaning 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.*”

Studies that are not greater than minimal risk and do not qualify for exempt classification may be given an expedited review by a CHR Co-Chair or a CHR member. Although an investigator may request an expedited review, CHR has final responsibility for determining the type of review required. All projects that involve greater than minimal risk are reviewed at a convened meeting of the full Committee at which a majority of the voting members are present.

Exempt Review

An exempt classification is only given to minimal risk research in one of the categories listed below. If the research falls into one of these categories, but is determined to be more than minimal risk, it may not be classified as exempt.

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular or special educational instructional strategies, or (ii) research on the effectiveness of, or the comparison among, instructional techniques, curricula, or classroom management methods. (45 CFR 46.101(b)(1)).

- (2) Research involving (a) educational tests, (b) survey or interview procedures or (c) 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 subject's financial standing, employability, or reputation. (45 CFR 46.101(b)(2)).
NOTE: When observation of public behavior includes children it can qualify as exempt research only if the investigator does not participate in the activities being observed. When research involving educational tests, or survey or interview procedures, includes children it cannot qualify as exempt research.
- (3) Research involving the use of education tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under category (2) above, 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. (45 CFR 46.101(b)(3)).
- (4a) Research involving the study of existing data, documents, records, pathological specimens, or diagnostic specimens, if the sources are publicly available. *Note: This item concerns publicly available data that contain identifiers or can be linked to specific individuals. "Existing" means that the data, documents, records or specimens were collected prior to submission of the research application.*
- (4b) Research involving the study of existing data, documents, records, pathological specimens, or diagnostic specimens, if the information, although initially containing identifiers, is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. (45 CFR 46.101(b)(4))
Note: This item concerns research on existing data, whether publicly available or not,, that has been recorded by the investigator in a manner that does not allow individual subjects to be identified or linkage to individual subjects to be reestablished. If these data, documents, records or specimens can be linked to specific individuals by any person, the research does not qualify as exempt research. Research on existing data, whether publicly available or not, that do not contain identifiers and cannot be linked to personal identifiers is not human research and does not require review by CHR.
- (5) Research and demonstration projects that 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 program; (iii) possible changes in or alternative to those programs or procedures; or (iv) possible changes in methods or levels of payments for benefits or services under those programs. (45 CFR 46.101(b)(5)).
According to the OHRP, this category applies only to Social Security benefit programs, procedures for obtaining benefits under those program, or possible changes in these programs.
- (6) Taste and food quality evaluation and consumer studies, if (i) wholesome food without additives are consumed, or (ii) 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. (45 CFR 46.101(b)(6)).

CHR does not conduct annual reviews of exempt research projects, but may, at its discretion, request periodic status reports. The investigator must notify CHR of any changes in the research plan that might affect the Committee's initial determination of exempt status. If, for example, analysis of an existing anonymized data set was initially classified as exempt, but the investigator now wishes to include analysis of an identifiable dataset, CHR must be notified and the change cannot be initiated without its prior approval.

Investigators conducting exempt research are bound to adhere to the ethical obligations outlined in the Belmont Report and 45 CFR 46. Informed consent must be obtained from all subjects regardless of the federal requirement, unless waived by CHR. Consent documents must be submitted with the CHR application for Certification of Exempt Status Research.

Expedited Review

Federal regulations recognize certain kinds of research, listed below, that are not more than minimal risk and that may be reviewed by an IRB through an expedited review process. Research that qualifies for expedited review is reviewed and approved by one or more CHR members (primary reviewers) or Co-Chairs and is not presented at a convened CHR meeting. All research approved under an expedited review procedure is re-reviewed at least annually. The reviewer may approve the project or recommend revision, but may not disapprove it. The CHR Co-Chair retains the right to require full Committee review, even for projects that appear to meet the criteria for expedited review. A monthly report of all research approved through an expedited review procedure is distributed to members at the full Committee meeting.

It should be noted that expedited review does *not* mean the review occurs any more quickly than a full Committee review.

If the proposed research is on the list below, it does not automatically mean it is eligible for expedited review. If any part of the proposed research is more than minimal risk, it must be reviewed by the full Committee. Research in any of these categories is *not* eligible for expedited review if the identification of subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, or reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are not greater than minimal.

Classified research is also *not* eligible for expedited review.

Criteria that determine whether research qualifies for expedited review apply regardless of the age of the subjects, except as noted below.

Activities 1-7 below apply to both *initial and continuing* expedited reviews.

- 1) Clinical studies of drugs and devices only under the following conditions:
 - a) Research on drugs or devices for which an investigational new drug (IND) exemption is not required, but *only* if the research does not significantly increase the risks, or decrease the acceptability of the risks, associated with use of the product.
 - b) Research on medical devices for which (i) an investigational device exemption (IDE) is not required (21 CFR 812), or (ii) the medical device is cleared or approved for marketing and the medical device will be used in accordance with its cleared or approved labeling.
- 2) Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows:
 - a) from healthy, non-pregnant adults, who weigh at least 110 pounds. (Amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more than 2 times per week.) or
 - b) from other adults and children, considering age, weight, and health, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. (The amount drawn may not exceed the lesser of 50 ml or 3 ml/kg in an 8-week period and may not occur more than 2 times per week.)
- 3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
 - a) hair and nail clippings, in a non-disfiguring manner;
 - b) deciduous teeth at the time of exfoliation;
 - c) permanent teeth if patient care indicates a need for extraction;
 - d) collection of excreta and external secretions (including sweat);
 - e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or applying a dilute citric solution to the tongue;
 - f) placenta removed at delivery;
 - g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
 - h) collection of both supra- and subgingival dental plaque and calculus, provided the collection procedure is accomplished in accordance with accepted prophylactic techniques;
 - i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; and
 - j) sputum collected after saline mist nebulization.
- 4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed they must be cleared or approved for marketing. Examples:

- a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
 - b) weighing or testing sensory acuity;
 - c) magnetic resonance imaging;
 - d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, echography, ultrasound, infrared imaging, doppler blood flow, and echocardiography; and
 - e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight and health of the individual.
- 5) Research involving materials (data, documents, records or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
 - 6) Collection of data from voice, video, digital or image recordings made for research purposes.
 - 7) Research on individual or group characteristics or behavior (including but not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.
 - 8) Continuing review of research previously approved by the convened IRB as follows:
 - a) the research is (i) permanently closed to the enrollment of new subjects, and (ii) all subjects have completed all research-related interventions, and (iii) the research remains active only for long-term follow-up of subjects; or
 - b) no subjects have been enrolled and no additional risks have been identified; or
 - c) the remaining research activities are limited to data analysis.
 - 9) Continuing review of research, not conducted under an IND application or IDE, where categories two (2) through eight (8) do not apply, *but* the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk *and* no additional risks have been identified.

Full Committee Review

Research that is more than minimal risk is reviewed at a convened meeting of the full Committee. In order to review the research, a majority of the voting members must be present, including at least one member whose primary concerns are in a non-scientific area. A physician must be present when reviewing FDA-regulated research. The Committee cannot review or approve research if a quorum fails during the meeting by recusal of members with conflicting interests, early departure, or absence of a non-scientist. A full Committee meeting may be cancelled for lack of quorum, lack of a non-scientific member, or other reasons determined by a Co-Chair.

Applications are placed on each Committee's agenda in the order in which they are received in the CHR Office. The schedule of full Committee meetings is available on the CHR website.

Application materials are sent to CHR members at least one week before the meeting. Those attending the meeting receive the application, the consent documents, and other materials, such as advertisements, interview scripts or recruitment letters. The primary reviewer also receives the complete grant application, sponsor's protocol, and questionnaires, and for an investigational drug or device study, the Investigator's Brochure. At the discretion of the Co-Chair, the investigator may be invited to attend the meeting to clarify unresolved issues. The investigator must, however, leave during the discussion and vote.

During the review, the primary reviewer summarizes his or her review of the project and states his or her recommendations. The Committee determines whether the project and proposed study methods meet the criteria for approval or whether revisions are required. The consent document is reviewed for accuracy, clarity, and inclusion of required and optional elements. By a majority of voting members present, the Committee may determine that the project is either:

- (1) approved, as submitted or with specified restrictions; or
- (2) disapproved, because the research was scientifically unsound or unnecessarily redundant, the risks outweighed the benefits, or the application was deficient to the extent that it required thorough rewriting before review was possible.

However, if the Committee requires additional information or requests revision of the proposal, it may vote to classify the status of review as either:

- (3) pending, back to reviewer, when the only requirement is the agreement of the investigator to specific requested changes or the completion of final administrative steps, such as receipt of local IRB approval or a certificate of translation for consent documents; in such cases, the Committee may delegate review and final approval to a Co-Chair or a single CHR reviewer under an expedited review procedure; or
- (4) pending, back to full committee. This classification is applied when questions are raised or revisions requested by the CHR that require the investigator's response and explanation, and subsequent review by CHR to determine if the issues raised have been satisfactorily resolved. This classification is also applied when the investigators do not agree to the specific changes requested for a proposal classified as pending, back to reviewer.

If a proposal is scheduled for review at a convened meeting of the full Committee, but the review is not done because a quorum was not present, a member was unable to present the study to the Committee, or time was not sufficient to complete the review, it will be classified as:

- (5) deferred, and would be reviewed at the next scheduled full committee meeting.

Written minutes of each full Committee meeting include: (1) attendance, (2) the number of votes to approve, defer, disapprove, or abstain, (3) the basis for requested changes or for disapproving the research, and (5) a summary of controversial issues and their resolution. Minutes are reviewed, revised as required, and approved at a subsequent full Committee meeting.

Review in Emergency Situations (TO BE ADDED)