

2.0 IRB REVIEW OF PROPOSED RESEARCH STUDIES - SUBMISSION REQUIREMENTS

The Institutional Review Board (IRB), University of Pittsburgh (University) must review and approve all research activities involving human subjects that fall under the University's human research protection program (see Preface) prior to the implementation of such research activities. There are three categories of IRB review of proposed research studies as discussed in Sections 2.1 - 2.3, below: 1) exempt review, 2) expedited review, and 3) full board review. Notification of the IRB Chair, or, in his absence, a physician Vice Chair, is required for the emergency use of a non-approved investigational drug or biologic or a non-approved investigational device (see Section 2.4).

2.1 Designation that a Project is Not Research, or is Research but Does Not Involve Human Subjects

Certain studies submitted for exempt review may not meet the University of Pittsburgh definition of human subject research because the activity meets neither the DHHS definition of human subjects research (i.e., does not meet the DHHS definition of "research" as specified under 45 CFR 46.102(d) involving "human subjects" as specified under 45 CFR 46.102(f)) nor the FDA definition of human subjects research. (i.e., does not meet the FDA definition of "research" as specified under 21 CFR 56.102(c) involving "human subjects" as specified under 21 CFR 56.102(e)). For example, Quality Assurance projects, may not meet the DHHS definition of "research" if they are not designed to develop or contribute to generalizable knowledge (45 CFR 46.102(d)) and do not meet the FDA definition of research if they do not involve the administration of drugs or devices (21 CFR 56.102(c)). Studies that are research, but do not involve human subjects (according to the regulations) might include those in which (a) the investigator conducting research neither interacts nor intervenes with an individual to obtain data (including specimens) about that person or (b) does not obtain identifiable private information. This determination is made by the Vice Chair for Exempt/Expedited reviews or his/her designee. Investigators apply for such a designation by completing the form "Request for a Determination that Planned Activity Does Not Involve Human Subjects Research" on the IRB website at www.irb.pitt.edu.

2.2 Exempt Review

Research activities in which the only involvement of human subjects will be in one or more of the categories listed below are exempt from the DHHS Federal Policy regulations (45 CFR 46.1.1(b)(1-6) including the requirement to obtain informed consent. However the exemption criteria at 45 CFR 46.101(b)(1-5) do not apply to research that is subject to FDA oversight (See Preface "definition of research). University policies require IRB review of human subject research activities appearing to meet these exempt criteria so as to ensure regulatory compliance. Research protocols qualifying for exempt review are reviewed administratively by the IRB Vice Chair for Exempt/Expedited Reviews or by his/her designee. Following an initial IRB determination of exempt status, exempt research activities are not subject to annual renewal requirements.

- 1) Educational practices (45 CFR 46.101(b)(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. This exemption does not apply to prisoners.

- 2) Surveys, questionnaires, interviews, observational studies (45 CFR 46.101(b)(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 research subjects can be identified (by the investigator or others), directly or through identifiers (codes) linked to the individuals; and (ii) any disclosure of the human research subjects' responses outside the research could reasonably place the individuals at risk of criminal or civil liability or be damaging to the individuals' financial standing, employability, or reputation. This exemption does not apply to research involving children, except for research involving the use of educational tests or research involving observation of public behavior of children (i.e., provided that the investigator(s) does not participate in the activities being observed). This exemption does not apply to research involving prisoners.
- 3) 45 CFR 46.101(b)(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 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. This exemption does not apply to research involving prisoners. IF YOU FEEL YOUR RESEARCH MEETS THIS CRITERION, PLEASE CONTACT THE IRB OFFICE.
- 4) 45 CFR 46.101(b)(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. In order to qualify for this exemption, the data/documents/records or specimens must be in existence (i.e., "on the shelf") at the time of protocol submission. This exemption does not apply to research involving prisoners.
- 5) 45 CFR 46.101(b)(5): Research and demonstration projects which are conducted by or subject to the approval of respective federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine.
 - a. Public benefit or service programs:
 - i. The program under study must deliver a public benefit (e.g., financial, or medical benefits as provided under the Social Security Act) or service programs (e.g., social, supportive, or nutrition services as provided under the Older Americans Act);
 - ii. The research or demonstration project must be conducted pursuant to specific Federal statutory authority;
 - iii. There must be no statutory requirements that the project be reviewed by an IRB; or
 - iv. The project must not involve significant physical invasions or intrusions upon the privacy of participants.
 - b. Procedures for obtaining benefits or services under those programs;

- c. Possible changes in or alternatives to those programs or procedures; or
- d. Possible changes in methods or levels of payment for benefits or services under those programs.
- e. This exemption is for projects conducted by or subject to approval of Federal agencies and requires authorization or concurrence by the funding agency.

This exemption does not apply to research involving prisoners. IF YOU FEEL YOUR RESEARCH MEETS THIS EXEMPTION CRITERION, PLEASE CONTACT THE IRB OFFICE.

- 6. 45 CFR 46.101(b)(6) and 21 CFR 56.104(d): Taste and food quality evaluation and consumer acceptance studies;
 - a. If wholesome foods without additives are consumed; or
 - b. 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.

This exemption does not apply to research involving prisoners. IF YOU FEEL YOUR RESEARCH MEETS THIS EXEMPT CRITERION, PLEASE CONTACT THE IRB OFFICE.

2.2.1 Exempt Review Submission Requirements

New exempt submissions are being processed through the University of Pittsburgh IRB's electronic submission process (OSIRIS). In order to submit an exempt application, please log onto www.osiris.pitt.edu and select the principal investigator and staff role and then click on "create new study." OSIRIS is designed as a series of branching questions that will guide you through the application process.

2.2.2 Exempt Review Turnaround Time

Research protocols qualifying for exempt review will be reviewed by the IRB Vice-Chair or his/her designee in order of the date submitted into the OSIRIS system. Depending upon the volume of submissions received, exempt review turnaround time varies.

2.3 Expedited Review

Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the categories listed below (carried out through standard methods) may be reviewed by the IRB through an expedited (i.e., administrative) review procedure. This means that these types of reviews are not conducted by an IRB committee, but rather administratively. **As defined by Federal Policy regulations, 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 (i.e., of the general public) or during the performance of routine physical or psychological examinations or tests.** Under an expedited review procedure, review of the research protocol and consent form is

carried out by the IRB Vice Chair for Exempt/Expedited Studies or his/her designee. In conducting the review, these individuals may exercise all of the authorities of the IRB except that they may not disapprove the research. A research activity may be disapproved only subsequent to full board review.

PLEASE NOTE THE FOLLOWING:

1. The expedited review procedure may not be used where identification of the 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, 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 no greater than minimal.
2. The expedited review procedure may not be used for classified research involving human subjects.
3. Standard requirements for informed consent (or its waiver, alteration or exception) apply to the research protocols qualifying for expedited review.
4. Requests for waivers of informed consent will, in general, require consideration at a convened meeting of an IRB committee.
5. Categories (1) through (7) below pertain to both initial and continuing review.

Research activities eligible for expedited review are limited by Federal Policy and FDA regulations to the following:

- 1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
 - a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

Note: Studies involving approved drugs typically constitute greater than minimal risk and thus cannot be expedited.

- b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

Note: Studies involving medical devices typically constitute greater than minimal risk and thus cannot be expedited.

- 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. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
 - b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently 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 nondisfiguring manner;
 - b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
 - c) permanent teeth if routine patient care indicates a need for extraction;
 - d) excreta and external secretions (including sweat);
 - e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by 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) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
 - i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
 - 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/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:
- a) physical sensors that are applied either to the surface of the body or at a distance and do not involve the input of significant amounts of energy into the individual or an invasion of the individual's privacy;
 - b) weighing or testing sensory acuity;
 - c) magnetic resonance imaging;
 - d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
 - 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 were initially collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis) and in which it will be possible for the investigators to identify directly or indirectly the respective research subjects.

- 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. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. See section 2.1, items 1, 2 and 4. This listing refers only to research that is not exempt).
- 8) Continuing review of research previously approved by the convened IRB as follows:
 - a) Where (i) the research is permanently closed to the enrollment of new subjects; (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) Where no subjects have been enrolled and no additional risks have been identified; or
 - c) Where the remaining research activities are limited to data analysis.

Note: Although permitted by the regulations to expedite a continuing review when no subjects have been enrolled, the University of Pittsburgh IRB will continue to have these studies reviewed by the full board unless one of the other above conditions are met.

- 9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories (2) through (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.

2.3.1 Expedited Review Submission Requirements

New expedited submissions are being processed through the University of Pittsburgh IRB's electronic submission process, OSIRIS. In order to submit an expedited application, please log onto www.osiris.pitt.edu and select the principal investigator and staff role and then click on "create new study." OSIRIS is designed as a series of branching questions that will guide you through the application process. In addition, please see Chapter 7 of the IRB Reference Manual, as well as the HELP text within the system, for suggestions on how to respond to the questions.

2.3.2 Expedited Review Turnaround Time

Research protocols qualifying for expedited review will be reviewed by the IRB Vice Chair for Exempt/Expedited Reviews or by his/her designee in order of stamp date received in the IRB office. Depending upon the volume of submissions received, expedited review turnaround time varies.

2.4 Full Board Review

Research activities which do not qualify for exempt review (see 2.1) or expedited review (see 2.2) under the stated categories must be reviewed and approved by a full IRB committee (full board) at a regularly scheduled meeting.

2.4.1 Full Board Review Submission Requirements

New full board submissions are being processed through the University of Pittsburgh IRB's electronic submission process, OSIRIS. In order to submit a full board application, please log onto www.osiris.pitt.edu and select the principal investigator and staff role and then click on "create new study." OSIRIS is designed as a series of branching questions that will guide you through the application process. In addition, please see Chapter 7 of the IRB Reference Manual, as well as the HELP text within the system, for suggestions on how to respond to the questions.

2.5 Emergency Use of Non-Approved and Investigational Drugs, Biologics or Devices: IRB Notification

The IRB chair and vice chairs are sometimes requested to expedite approval (i.e., outside of an ongoing IRB-approved research protocol) of the emergency use of a non-approved or investigational new drug (including a biologic) or device in a patient who is desperately ill and for whom no standard alternative therapies exist.

2.5.1 Emergency Use/Emergency IND (see Appendix B, Requirements and Procedures for the Emergency Use of a Non-approved or Investigational Drug, Biologic, or Device):

FDA regulations and guidelines for the protection of human research subjects allow for a non-approved or investigational drug or device to be used in emergency situations without prior IRB approval. Emergency use is defined by these regulations as a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB (i.e., full board) approval. The emergency use provision in the FDA regulations is an exemption from the standard requirement for prior review and approval by a convened IRB committee. This exemption, which may not be used unless all of the conditions described above are met, allows for emergency use of the non-approved drug or device for only one patient. FDA regulations and University policy require that any additional human use of the non-approved drug or device subsequent to the initial, exempted emergency be conducted under a research protocol subject to prospective IRB (i.e., full board) review and approval and FDA approval of a corresponding IND or IDE application.¹ An investigator cannot carry out a research project on a case-by-case basis under an emergency use premise.

- University policies require that the IRB chair or a physician vice chair be notified prior to the emergency use of a non-approved drug or device; however, this notification should not be construed as an IRB approval. Notification of the IRB chair or physician vice chair is required to ensure that the conditions described in the respective federal regulations are met.
- **The emergency use of a non-approved or investigational drug or biologic requires an IND (investigational new drug) exemption.** If the intended subject/emergency use does not meet the eligibility criteria or methods of a clinical trial being conducted under a currently approved IND for the drug or biologic, the

¹The responsible federal agencies and University acknowledge, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that there has not been sufficient time to convene an IRB meeting to prospectively review and emergency use research protocol.

physician must contact the FDA to obtain permission prospectively for the emergency use under this previously approved IND (see Appendix B, Requirements and Procedures for the Emergency Use of a Non-Approved or Investigational Drug, Biologic, or Device). If there is currently no IND in place for the non-approved drug or biologic, the physician must contact the FDA to obtain prospectively an Emergency IND number. Alternately, the emergency use may be conducted under an existing Treatment IND or Parallel Track IND (see pages P-8 and P-9). The physician should contact the sponsor (manufacturer) of the investigational drug or biologic to ascertain its IND status and/or whether a Treatment IND or Parallel Track IND exists for the drug/biologic.

Even for an emergency use, the investigator is required to obtain (i.e., in advance of the use) the informed consent of the patient or the patient's legally authorized representative (see example of Emergency Use Consent Form, Appendix B).

2.6 Emergency Use of Approved Drugs or Biologics for "Off-Label" Indications: IRB Notification (see Appendix C)

Good medical practice and patient interests require that physicians be able to use approved (i.e., marketed) drugs and biologics according to their best knowledge and judgment. If a physician uses, for the care of an individual patient, an approved product for a treatment or diagnostic indication that does not appear in its approved labeling (i.e., an "off-label" indication), s/he has the responsibility to be well informed about the product, to base such use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. (Note the USP-DI, U.S. Pharmacopeial Convention Inc., Rockville, MD, is a federally recognized source of information on well-established "off-label" indications.)

The emergency "off-label" use, for the care of an individual patient, of an approved drug or biologic in the manner described above is considered the "practice of medicine" and does not require notification of the IRB.