

## **PARTNERS HUMAN RESEARCH COMMITTEE POLICIES AND PROCEDURES**

### **Initial and Continuing Review of Human-Subjects Research and Proposed Minor Changes in Approved Research Using the Expedited Review Procedure**

#### **1.0 PURPOSE**

The purpose of this policy is to define the procedures the Partners Human Research Committees (PHRC) follow when conducting initial and continuing review of non-exempt human-subjects research and clinical investigations and review of proposed minor changes in approved research using the expedited review procedure.

This policy is established to comply in part with the regulatory requirement in 45 CFR 46.103(b)(4)(i) and 21 CFR 56.108(a)(1) requiring IRBs to have “written procedures which the IRB will follow for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution.”

#### **2.0 SCOPE**

Non-exempt human-subjects research and clinical investigations reviewed by the PHRC Chairpersons using the expedited review procedure are subject to this policy.

#### **3.0 DEFINITIONS**

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of *research* and *human subject* and/or the FDA definitions of *clinical investigation* and *human subject*. The DHHS definition for *research* and *human subject* and the FDA definition for *clinical investigation* and *human subject* are provided below.

*Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

*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. [45 CFR 46.102(f)(1)(2)]

*Clinical investigation* means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous... [21 CFR 50.3(c) and 21 CFR 56.102(c)]

*Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

*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. [45 CFR 46.102(i)][21 CFR 56.102(i)]

#### 4.0 POLICY

The PHRC may use the expedited review procedure for review and approval of certain categories of human-subjects research that involve no more than minimal risk, and for review and approval of minor changes in approved research during the period of IRB approval [DHHS in 45 CFR 46.110 and FDA in 21 CFR 56.110]. When reviewing non-exempt human-subjects research and clinical investigations using the expedited review procedure, the PHRC Chairpersons are subject to the *Partners Conflicts of Interest Policy for IRB Members*.

## 5.0 PROCEDURES

Investigators relying on the PHRC for IRB review of human-subjects research and clinical investigations are required to complete application forms and provide all required information and documents to the Partners Human Research Office for review by the PHRC as described in the *Protocol Submission Instructions*, *Continuing Review Instructions*, and applicable forms.

### 5.1 Initial Review and Continuing Review

5.1.1 All of the required forms and documents submitted by the investigator for review and, when previously reviewed, the PHRC study file are provided by the Human Research Office staff to the PHRC Chairperson for review. When the study files consists of many volumes, the most recent volume is provided. Prior volumes of PHRC study files are available in the Human Research Office and are provided to reviewers, upon request. Additionally, the PHRC Chairpersons have access to the PHRC database that contains the complete review history.

1.1.1 Continuing review of the research is required until the research has been completed or has been closed prior to completion. The investigator must submit the continuing review form to document that the study has been completed or is being closed prior to completion. For multi-site research, the research may be considered completed or may be closed prior to completion when the investigator at this site is no longer collecting, receiving, or analyzing identifiable data.

5.1.2 Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the PHRC through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110 [Source: 63 FR 60364-60367, November 9, 1998]. The categories in this list apply regardless of the age of subjects, except as noted:

#### Research Categories:

- (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: Research on marketed drugs that significantly increase the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

- (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.
- (2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
  - (a) from healthy, nonpregnant 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 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, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate give 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 nonresearch purposes (such as medical treatment or diagnosis). [Note: Research involving materials that have been collected includes materials collected for both research and nonresearch purposes per personal communication with Julie Kaneshiro of OHRP April 2003].
- (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) where (i) the research is permanently closed to the enrollment of 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.
- (9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption 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.

- 5.1.3 Research in any of these categories may require review at a convened meeting of the PHRC if the circumstances of the proposed research involve more than *minimal risk*.
- 5.1.4 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 the risk related to invasion of privacy and breach of confidentiality is no greater than minimal.
- 5.1.5 In addition, the expedited review procedures may not be used for classified research involving human subjects. Classified research is research that has a security classification established by an authorized agency of the federal government. BWH and MGH do not conduct classified research.
- 5.1.6 The PHRC Chairpersons are responsible for reviewing and determining whether the research is eligible for review using the expedited review procedure. The reviewing PHRC Chairperson uses a form listing the expedited review categories published in the Federal Register at 63 FR 60364-60367 to document:
- That the research is minimal risk;
  - The applicable research categories; and
  - That the consent form includes the basic elements of informed consent or that a waiver or alteration of informed consent is approved.
- 5.1.7 If the proposed research is not eligible for review using the expedited review procedure, the reviewing PHRC Chairperson requests the research activity be scheduled for full board review at a convened meeting of the PHRC.
- 5.1.8 The reviewing PHRC Chairperson may approve, require modifications in (to secure approval), or defer action pending receipt of additional information from the Principal Investigator (PI). The reviewing PHRC Chairperson may not disapprove a study using the expedited review procedure; protocols can only be disapproved by the PHRC at a convened meeting.

- 5.1.9 The reviewing PHRC Chairperson may consult another PHRC member(s) or a non-PHRC member consultant with special scientific or scholarly expertise in the scientific area or discipline or special population being studied; however the reviewing PHRC Chairperson is responsible for the review and approval of research using the expedited review procedure. When a consultant is used, the reviewing PHRC Chairperson or designated is responsible for communicating with the consultant and for verifying that the consultant does not have a conflict of interest as defined in the *Partners Conflicts of Interest Policy for IRB Members*.
- 5.1.10 When the reviewing PHRC Chairperson requires modifications in the research to secure approval or defers action pending receipt of additional information, the Human Research Office notifies the PI in writing of the required modifications or additional information required for review. The PI is asked to submit a point-by-point response and revised documents to the PHRC within 60 days of the review date. Unless the PI requests an extension or there are extenuating circumstances, the research is withdrawn from further review at the end of the 60-day period if no response is received.
- 5.1.11 When received, the reviewing PHRC Chairperson reviews the PI's response, including revised documents, and determines whether the modifications have been made as requested and the research can be fully approved. The reviewing PHRC Chairperson may continue to request additional modifications or information until the research is approved or referred for full board review at a convened meeting of the PHRC.
- 5.1.12 When the human-subjects research is reviewed using the expedited review procedure, the reviewing PHRC Chairperson is responsible for determining that all of the requirements set forth in 45 CFR 46.111 and, when applicable, 21 CFR 56.111 are satisfied.
- 5.1.13 When the human-subjects research is reviewed using the expedited review procedure, the date of expiration of PHRC approval is automatically one year from the date of PHRC approval. PHRC approval expires as of that date.
- 5.1.14 Independent verification of information provided at initial or continuing review, or for review of proposed changes in research during the period of approval may be requested by the reviewing PHRC Chairperson in the course of conducting the review. Such independent verification may be considered in the following situations:
- research being conducted by persons who have previously failed to comply with all regulations;

- research conduct that comes in question as a result of information provided at continuing review; or
- research in which substantial segments of the project are conducted off-site by Partners investigators or collaborators.

Independent verification may include, but are not limited to:

- audit by the Human Research Quality Improvement Program;
- communications between the FDA and the sponsor/IND holder
- communications from any monitoring group, e.g., DSMB or DMC
- GCRC evaluations and reviews;
- NIH communications and reviews; and/or
- communications with collaborating IRBs.

## 5.2 Minor Changes in Approved Research

- 5.2.1 The reviewing PHRC Chairperson is responsible for reviewing and determining whether the proposed change (or amendment) is minor, and if minor, may review and approve the change using the expedited review procedure described above.
- 5.2.2 The proposed change is considered minor when the research meets all of the following criteria:
- the proposed change does not significantly alter the risk to benefit assessment the PHRC relied upon to approve the protocol;
  - the proposed change does not significantly affect the safety of subjects;
  - the proposed change does not involve the addition of invasive procedures (procedures not otherwise eligible for expedited review, e.g. collection of blood samples in limited amounts);
  - the proposed change does not involve the addition of procedures, interactions or interventions that add significant medical, social or psychological risks;
  - the proposed change does not involve addition of a vulnerable population in research not otherwise eligible for expedited review; and
  - the proposed change does not significantly alter the scientific question or the scientific quality of the study.
- 5.2.3 The reviewing PHRC Chairperson, document approval using a review form that includes the rationale for approving the change using the expedited review procedure. The reviewing PHRC Chairperson may request additional information from the PI to make this determination.

### 5.3 Notification of Principal Investigators, PHRC Members, and Institution

- 5.3.1 The Human Research Office is responsible for notifying the Principal Investigators in writing of PHRC approval of initial or continuing review, or proposed changes in research activities during the period of approval. The approval letter includes the date of expiration of PHRC approval.
- 5.3.2 The Human Research Office is responsible for preparing and distributing a report of all human-subjects research approved using the expedited review procedure, including initial and continuing review, and proposed changes in approved research during the period of PHRC approval. The report is distributed with the agenda and meeting materials for convened PHRC meetings.
- 5.3.3 The expedited agenda reports are made available electronically to the Institutional Officials in a shared file area. In addition, the Human Research Office provides individuals and/or departments within Partners with responsibility for some aspect of the human research protection program electronic access to PHRC review information via the Insight Research Portal.