

JURISDICTION, STRUCTURE, AND RESPONSIBILITIES OF THE INSTITUTIONAL REVIEW BOARD

Institutional Review Board of the University of Pittsburgh

The Institutional Review Board (IRB) of the University of Pittsburgh (FWA00006790) is an appropriately constituted administrative body established to protect the rights and welfare of human subjects (including patients) recruited to participate in research activities. In accordance with the Federal Policy regulations (45 CFR 46) of the Department of Health and Human Services (DHHS) and the applicable regulations (21 CFR 50, 56) of the Food and Drug Administration (FDA), the IRB has the authority to approve, require modifications in (in order to approve), or disapprove all research activities involving humans. The University of Pittsburgh's human research protection program encompasses all human subject research wherein University of Pittsburgh faculty, students, staff or facilities are engaged¹ in the conduct of the research or the human subject research involves the private records² of the University of Pittsburgh; with the following exceptions:

- 1) VA Pittsburgh Healthcare System (VAPHS): The University of Pittsburgh executed (May 2005) a revised Memorandum of Understanding (MOU) with the VAPHS which outlines the IRB review and approval requirements for human subject research studies that are jointly subject to oversight by the IRBs of these institutions (see Appendix F). As per item 1.a. of the General Procedures section of this MOU:

"The VAPHS IRB shall be the IRB-of-Record for all human subject research studies in which: a) a VAPHS staff member or University faculty member is the principal investigator or a co-investigator of the study; b) the research is conducted using only VAPHS records and/or research subjects recruited through the VAPHS; c) no University or UPMC facilities are engaged in the conduct of the research; and d) no University funds are expended in direct support of the research."

Human subject research subject solely to review and approval by the VAPHS IRB, in accordance with item 1.a. of the General Procedures section of this MOU, is not part of the University of Pittsburgh's human research protection program; i.e., it is part of the VAPHS's human research protection program. Human subject research that falls under items 1.b and 1.c of the General Procedures section of this MOU requires University of Pittsburgh IRB review and approval and, hence, remains part of the University of Pittsburgh's human research protection program.

- 2) UPMC Clinical Trials Office (UPMC CTO): Effective August 24, 2004, the University of Pittsburgh and the UPMC entered into an agreement whereby, with certain limited exceptions, all industry-initiated and sponsored clinical trials conducted within UPMC or UPP facilities by University faculty or staff, who are also UPMC or UPP staff members, became the responsibility of the UPMC, and will be processed through the UPMC CTO. Therefore, industry-initiated and sponsored clinical trials conducted by University faculty and staff and subject to the terms of this agreement are not part of the University of Pittsburgh's human research protection program; i.e., they are part of the UPMC's human research protection program.

¹ "Engaged in the conduct of the research" shall be defined in accordance with the current Office of Human Research Protection (OHRP guidance).

² The University of Pittsburgh will treat all IRB records under University policy 10-02-06 as "internal use only" data. While the University of Pittsburgh is a state related University, it is not subject to the Pennsylvania Right-to-Know Law.

Affiliated Institutions:

1. UPMC Institutions: Through a collaborative agreement dated December 15, 2003, the UPMC has delegated authority to the University of Pittsburgh IRB to review initially and periodically and to approve, require modifications in (to secure approval) or disapprove all human subject research wherein UPMC or UPP (PSD)³ staff or facilities are engaged in the conduct of the research or the human subject research involves the private records of the UPMC or UPP (PSD); with the exception of industry-sponsored clinical trials processed through the UPMC Clinical Trials Office (see A.2), above).
2. UPMC Children's Hospital of Pittsburgh (CHP): Through a collaborative agreement dated April 1, 2004, the CHP has delegated authority to the University of Pittsburgh IRB to review initially and periodically and to approve, require modifications in (to secure approval) or disapprove all human subject research wherein CHP staff or facilities are engaged in the conduct of the research or the human subject research involves the private records of the CHP.
3. Magee Women's Research Institute (MWRI): Through a collaborative agreement dated April 1, 2004, the MWRI has delegated authority to the University of Pittsburgh IRB to review initially and periodically and to approve, require modifications in (to secure approval) or disapprove all human subject research wherein MWRI staff or facilities are engaged in the conduct of the research or the human subject research involves the private records of the MWRI.

Other Institutions

In the absence of a Cooperative Agreement, human subject research conducted by University faculty, students or staff or UPMC staff at another institution will require review and approval by both the University IRB and the institutional review board of the other institution. To expedite the approval process, it is recommended that approval of the external institutional review board be obtained prior to submitting the research protocol to the University IRB. The University IRB will accept the specific format requirements of the external institution provided that the general requirements, as outlined in this reference manual, are appropriately addressed. If the other institution does not have an institutional review board, approval of the University IRB may be the only IRB-approval requirement depending on the nature of the activities to be conducted at the other institution and specifying that all institutional commitments and regulations, applicable laws, and standards for professional conduct and practice have been appropriately addressed by the investigators.

Note: If human subject research will be conducted in or involving the staff, patients, students, etc. of an institution which has not executed a Cooperative Agreement with the University of Pittsburgh IRB and which does not have its own institutional review board, the respective University IRB application must include a letter from a responsible administrator of the institution indicating his/her permission for the research to be conducted at the institution.

Other Institutions – Assurance Agreements

The conduct of Federally-supported human subject research at another institution is subject to the requirement that the other institution have in place a FederalWide Assurance (FWA) agreement with OHRP. If the other institution does not have an FWA in place, it may be required (i.e., depending on the nature of the research activities to be conducted at the institution) to execute a FWA agreement with OHRP prior to the conduct of the research at that site. Contact the IRB Office for clarification of this requirement as it pertains to the specific research activities to be performed at the other institution.

³ UPP (PSD) means the University of Pittsburgh Physicians (Physician Service Division) practice plan, UPMC.

Structure of the IRB

The University IRB is currently comprised of ten IRB committees, each functioning as a separate IRB under centralized management by, and with support from, the IRB Office. Each IRB committee is directed by an IRB vice chairperson, and is comprised of members with multidisciplinary expertise and backgrounds as required by the Federal Policy and FDA regulations. In addition, the IRB Office staff includes an IRB vice chair and research review coordinators dedicated to the review and approval of research studies that qualify for exempt or expedited (i.e., administrative) review status.

Purpose of the IRB

The purpose of IRB review is to assure, both in advance and by periodic monitoring, that appropriate steps are taken to protect the rights and welfare of human research subjects. The focus of the IRB review process is to ensure that:

- 1) the risks to human research subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose the research participants to risk, and whenever appropriate, by using procedures already being performed on subjects for diagnosis or treatment purposes.
- 2) the risks to human research subjects are reasonable in relation to the anticipated benefits (if any) to the individual, and the importance of the knowledge that may be expected to result.
 - For the purpose of IRB consideration, "benefit" is defined as a valued or desired outcome; an advantage.
 - For the purpose of IRB consideration, "risk" is defined as the probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. In evaluating risk, the IRB is to consider the conditions that make the situation dangerous, per se (i.e., as opposed to those chances that specific individuals are willing to undertake for some desired goals).
 - In evaluating risks and benefits, the IRB considers only those risks and benefits that may result from the research (i.e., as distinguished from risks and benefits of treatments or procedures that the patient would undergo if not participating in the research).
 - In evaluating risks and benefits, the IRB does not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of research on public policy).
- 3) the selection of human subjects for research participation is equitable.
- 4) human research subjects are adequately informed of the risks and benefits of research participation and the procedures that will be involved in the research; and that informed consent is obtained from each prospective human research subject, or his/her legally authorized representative, in accordance with, and to the extent required by federal regulations and IRB policies.
- 5) informed consent of human research subjects is obtained in advance of research participation and appropriately documented in accordance with, and to the extent required by federal regulations and IRB policies.
- 6) the research plan, when appropriate, makes adequate provisions for monitoring the data collected to ensure the safety of human research subjects.
- 7) there are adequate provisions to protect the privacy of human research subjects and to maintain the confidentiality of research data.
- 8) appropriate additional safeguards have been included in the study to protect the rights and welfare of human research subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, decisionally impaired persons, or economically or educationally disadvantaged persons).

IRB Office Staff and Responsibilities

Chairman - Has ultimate responsibility for the review/approval of human subject research conducted under the jurisdiction of the University of Pittsburgh IRB.

Director, IRB Office - Has oversight responsibility for the administration and operation of the IRB Office. Responsible for ensuring IRB and IRB Office compliance with Federal and state regulations and institutional policies governing human subject research and human subject research protections. Provides education and support to the research community.

Legal Counsel - Advises the Vice Chancellor for Research Conduct and Compliance (the Authorized Institutional Official), the IRB Chairman, the Director of the IRB Office, and the IRB Executive Committee on legal issues related to human subject protections and the functions and activities of the IRB and IRB Executive Committee.

Committee Vice Chairpersons - Conduct IRB meetings and review and approve the meeting minutes. Physician Vice Chairs are also on-call for emergency use notifications.

Exempt/Expedited Vice Chairperson – Oversees the administrative (i.e., IRB Office) review and approval of research studies qualifying for exempt or expedited review status.

IRB Assistant Director: Has responsibility for ensuring compliance with federal regulations as well as internal policies and procedures. Oversees communication respective to Federal Wide Assurance agreements, InterInstitutional Amendments and Cooperative Agreements. Responsible for maintaining and updating IRB policies and procedures and the IRB Reference Manual. Provides education and support to the research community as well as to the IRB staff.

IRB Office Manager - Provides management and oversight of IRB office functions. Responsible for supervision of IRB office staff. Assist with development, implementation, and monitoring of policies and procedures. Maintains up-to-date information regarding federal regulations and IRB policies related to the use of human subjects in research.

Protocol Processing Coordinators: Responsible for the processing of human subject research applications submitted to the IRB Office to include: database entry, development of IRB committee agendas, preparation of IRB committee review materials, protocol filing, etc. Provide education and support to the research community.

Education Coordinator: Responsible for initial education, orientation and continuing education of IRB committee members. Responsible for human subject protection educational programs directed at research investigators. Responsible for educating research investigators and staff regarding IRB application processes. Provides education and support to the research community.

Research Review Coordinators: Responsible for reviewing, as delegates of the IRB Chair and/or designated IRB committee members, human subject research applications. Responsible for attending convened IRB committee meetings, ensuring compliance with IRB policies and procedures, and documenting meeting activities and decisions (i.e., meeting minutes). Provide education and support to the research community.

Adverse Event Coordinator: Reviews and coordinates the IRB review and response to all reports of adverse events which occur in conjunction with the conduct of human subject research studies approved by the University of Pittsburgh IRB. Provides education and support to the research community.

IRB Member Coordinator: Responsible for the identification of IRB members, maintaining up-to-date membership rosters with OHRP, assisting with the orientation of new board members and providing continuing education at IRB board meetings.

IRB Regulatory Coordinator: Responsible for special projects identified by the Office of the Director. This includes preparing new guidance documents for the research community, working with the OSIRIS team to identify areas of improvement, and acting as the coordinator for Committee F (Executive Committee).

IRB Committee Members: Responsible for the review and approval of human subject research applications requiring consideration by a convened IRB committee. Note: If required for submission to a research sponsor, a current listing of the IRB committee members is available from the IRB Office.

DEFINITIONS OF RESEARCH AND HUMAN SUBJECTS

The University of Pittsburgh IRB is required to review and approve all research activities involving human subjects prior to their implementation. There is sometimes a question of whether a planned activity is "research involving human subjects" and, therefore, requires IRB review and approval.

University of Pittsburgh Definition of Human Subject Research

Under the Organization's policies and procedures an activity is human subject research if it is either (1) human subject research subject to FDA regulation or (2) human subject research subject to DHHS regulations.

DHHS Definition of Human Subject Research:

Activities are human subject research subject to DHHS regulations when they meet the DHHS definition of "research" and involve one or more "human subjects" as defined in DHHS regulations

Research as defined by HHS regulations (45 CFR 46.102) shall mean a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. As defined in the Belmont Report, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships).

Human subjects are defined by HHS Regulations at 45 CFR 46.102(f) as "a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or 2) identifiable private information." Intervention includes both the physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact (e.g., questionnaires, interviews) between the investigator and the 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.

FDA Definitions of Human Subject Research:

Activities are human subject research subject to FDA regulations when they meet the FDA definition of "research" and involve one or more "human subjects" as defined in FDA regulations

Under FDA Regulations (56.102) the term “clinical investigation” is synonymous with “research” and means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i), or 520(g) of the Federal Food, Drug and Cosmetic Act (“the Act”), or need not meet the 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 later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. Clinical investigations regulated by the FDA under Sections 505(i) and 520(g) of the Act, include investigations of foods, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. The term “clinical investigation” does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. Research is subject to 21 CFR Parts 50 and 56 when it involves the use of any drug other than the use of an approved drug in the course of medical practice. Research is subject to 21 CFR Parts 50 and 56 when it involves the use of any medical device other than the use of an approved medical device in the course of medical practice.

Human subject is defined under FDA regulations at 21 CFR 50.3(g) as “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 individual or a patient.” If the research involves a medical device, human subjects are individuals when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR §812.3(p)).

Innovative Practice versus Research

Innovative or newly-introduced clinical procedures or therapies do not require IRB review and approval except when they involve “research” as defined by the above criteria. An innovative clinical practice is an intervention designed solely to enhance the well-being of an individual patient or client. The purpose of an innovative clinical practice is to provide diagnosis, preventative treatment, or therapy to particular individuals. The introduction of innovative procedures or therapies into clinical practice (i.e., independent of a research activity approved by the IRB) should be reviewed with the applicable department chairperson and the UPMC Technology Assessment Committee/Innovative Practices Sub-Committee prior to their implementation (contact Juliet Jegasothy at 412-454-7490).

Quality Assurance Projects versus Research

Quality assurance projects do not require IRB review and approval except when they involve “research” as defined by the above criteria. Precise definitions to permit the distinction between research studies and quality assurance projects are difficult and have not been established. In general, a quality assurance project is a project that is focused primarily on improving patient care within a given patient care environment [e.g., hospital or health care organization] and, as such, the outcome of the project may not be generalizable to other patient care environments. Publication of a quality assurance project does not, per se, render that project “research”; however, if the outcome of a quality assurance project is published, attention should be given to avoiding the terminology “research” in the publication. Listed below are questions directed at providing guidance in distinguishing quality assurance projects from research:

- Is there a commitment, in advance of data collection, to a corrective plan given any one of a number of study outcomes? Does the principal investigator of the study have both clinical supervisory responsibility and the authority to impose change?
 No* Yes *If no (i.e., to either question), the study requires prior review and approval by the University of Pittsburgh IRB.

- Is the research being sponsored/funded by an external agency?
 No Yes* *If yes, the study MAY require prior review and approval by the University of Pittsburgh IRB.
- Does the proposed study involve the prospective assignment of patients to different procedures or therapies based on a predetermined plan such as randomization?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.
- Does the proposed study involve a “control group” in whom the therapeutic or study intervention is intentionally withheld to allow an assessment of its efficacy?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.
- Will the study intervention be delivered in a blinded fashion wherein neither the physician nor the patient knows to whom the study intervention or comparative intervention (e.g., placebo, standard care) was given?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.
- Is the assessment of outcome blinded to the study intervention for the purpose of establishing the efficacy of the intervention?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.
- Does the proposed study involve the prospective evaluation of a drug, biologic or device that is not currently approved for general use by the FDA (i.e., to include evaluations of off-label indications)?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.
- Will patients involved in the proposed study be exposed to additional risks or burdens (i.e., other than the completion of patient satisfaction surveys) beyond standard clinical practice in order to make the results of the study generalizable?
 No Yes* *If yes, the study requires prior review and approval by the University of Pittsburgh IRB.

Note that to address this issue both UPMC and CHP have adopted an oversight process that requires the submission of all quality assurance projects for review. At UPMC, submissions are reviewed by the Total Quality Council. The contact person is Juliet Jegasothy at 412-454-7490. At CHP, submissions are reviewed by the CHP Quality Improvement Committee. The contact person is Lorina Wise, Esq. at 412-692-8073.

Research On or Involving Deceased Individuals

Research performed on individuals who have been declared legally dead and/or research involving the collection of tissues from deceased individuals is not subject prior review and approval by the University of Pittsburgh IRB. (Note that the Federal Policy regulations governing human research subject protections defines a “human subject” as “a living (*emphasis added*) individual about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information.) There are, however, ethical issues associated with research conducted on or involving deceased individuals. To address these ethical issues, all University faculty who desire to perform research on or involving deceased individuals must submit a project application for review and approval by the Committee on Research Involving the Dead (CORID, contact Shoshana Matusak at 412-802-8280). Note that, as per UPMC policies, research involving the medical records of deceased individuals is subject to obtaining the written consent of the decedents’ next-of-kin or the executors of the decedents’ estates. For studies that include BOTH living and deceased subjects, the IRB is the institutional committee with jurisdiction for oversight and approval.