

**Washington University
Institutional Review Board
Policies and Procedures**

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I. Authority and Institutional Commitment

- A. The Executive Vice Chancellor for Medical Affairs and Dean (EVC/Dean) of the Washington University School of Medicine (WUSM) and the Vice Chancellor for Research (VCR) for Washington University (WU) are the authority under which the WU Institutional Review Board (IRB) is established and empowered.
- B. The WU IRB holds a Federalwide Assurance (FWA00002284), approved by the Office for Human Research Protections (OHRP). This assurance applies to all non-exempt research involving human subjects funded by federal agencies subscribing to the Common Rule.
- C. WUSM is affiliated with Barnes-Jewish Hospital and Saint Louis Children's Hospital. The WU IRB serves as the IRB of record under their respective assurances with OHRP: Barnes-Jewish Hospital (FWA00002281) and Saint Louis Children's Hospital (FWA00002282) WU, Barnes-Jewish Hospital, and Saint Louis Children's Hospital are hereafter referred to collectively as WU/BJH/SLCH.
- D. The mission of the IRB is to protect the rights and welfare of participants in "human research" as defined in 45 CFR 46.102(d) and (f) and "clinical investigations" as defined in 21 CFR 50.3(c).
- E. All of the human research activities and all activities of the IRBs designated in the WU Federal Wide Assurance (FWA), regardless of sponsorship, are guided by the ethical principles in "The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research."¹
- F. When appropriate, all collaborating institutions and investigators engaged in non-exempt human research, as defined in Section II(A) of this policy, will operate under an OHRP or other federally approved Assurance for the protection of human subjects.²
- G. When any research covered by this Policy takes place in a foreign country, the procedures prescribed by the international institution, if any, will afford protections that are at least equivalent to those provided in this Policy and the research design will consider the local research context where research procedures will occur.³ The PI/PD must retain in the research record current, written documentation of any approvals that may be required, a copy of which will be made available upon request.
- H. Except for research exempted under 45 CFR 46.101(b), exempted under WU's Category 2a exemption for non federally funded studies (as defined in the glossary) or waived in accordance with 45 CFR 46.101(i), all human research will be reviewed, prospectively approved, and subject to continuing oversight and review at least annually.⁴ The IRB has the authority to:
 - 1. approve, require modifications, or disapprove all research activities that fall within its jurisdiction;⁵

2. suspend, place restrictions, or terminate approval of research activities that fall within its jurisdiction that are not being conducted in accordance with IRB requirements or that have been associated with unanticipated problems;
 3. observe or have a third party observe the consent process and/or the conduct of the research if the IRB determines it to be indicated.
- I. The IRB will report actions and findings to appropriate institutional officials by making available to the WU and BJH Medical Executive Committees all committee meeting minutes for review. Statistical statements will be reviewed by the BJH Medical Executive Committee at least annually and statistics of IRB actions will be presented to the WU Advisory Board and the Executive Committee at least annually. The Executive Chair presents an annual report to the WUSM Medical Executive Committee and the WU Advisory Board. The WUSM Medical Executive Committee is comprised of all WUSM Department Chairs, BJH officials, the WUSM Dean, General Counsel, and unaffiliated members. The WU Advisory Board is chaired by the Vice Chancellor for Research. Membership consists of the Deans of Arts and Sciences, Social Work and School of Medicine, the Chair of Psychology, the Chair of the WUSM Research Committee and the Executive Vice Chancellor for Administration. Reports, actions, and statistics are provided to other institutional officials, as needed.
 - J. The IRB functions independently of, but in collaboration with, University officials and other WU/BJH/SLCH committees. Research that has been reviewed by the IRB may be subject to further review and approval or disapproval by officials of WU/BJH/SLCH; however, these officials may not approve research if it has been disapproved by the IRB.⁶
 - K. The VCR is the Institutional Official on the WU Federalwide Assurance and is responsible for oversight of the WU human research protection program. The EVC/Dean is responsible for the operational oversight of HRPO and selects and appoints the Executive Chair for an unlimited term of appointment. The Executive Chair is responsible for exercising appropriate oversight to ensure that the IRB is in compliance with policies and procedures for protecting human research participants and reporting to the EVC/Dean quarterly. The EVC/Dean has the authority to remove or replace the Executive Chair.⁷
 - L. WU will make provisions for adequate meeting space and staff necessary to support the IRB's review and record keeping duties.⁸
 - M. The IRB will review protocols to ensure compliance with the HIPAA Privacy Rule, 45 CFR Parts 160 and 164.
 - N. The WU Chancellor prohibits officials, investigators, employees, and sponsors from attempting to exercise undue influence over any of the IRB members, staff of the Human Research Protections Office (HRPO), or any other member of the research team to obtain a particular result, decision, or action.
 - O. If an IRB committee member, principal investigator/project director (PI/PD), research participant, or other individual feels that he/she has been unduly influenced or coerced (e.g., to participate, approve a study, or conduct a study), a

report should be made to the Executive Chair, VCR, or through the University Compliance Hotline (314-362-4998). Such reports will be reviewed and investigated by the Executive Chair, and, when appropriate, corrective actions will be taken. If the Executive Chair is involved in the allegation of undue influence or coercion, the VCR will be responsible for the investigation.

- P. Appeals related to IRB policies and procedures (including investigator concerns or suggestions regarding the IRB review process) will be referred to the Executive Chair who will triage the issue/concern. Mechanisms for addressing the concern could include:
1. appointment of an ad hoc committee of representative faculty, IRB members, HRPO staff, and others appropriate to advise on the particular issue;
 2. referral to the IRB Chair's Advisory Committee;
 3. other appropriate forums identified by the Executive Chair to address a specific concern; or
 4. dismissing the concern as outside the latitude allowed by the federal regulations or accreditation standards.

II. Applicability: Activities Subject to IRB Jurisdiction

- A. All instances where WU/BJH/SLCH engages in human research must be reviewed and approved by the IRB prior to initiation. Engagement encompasses all activities whereby any WU/BJH/SLCH employee (including faculty or staff), agent, student, fellow, or post-doctoral appointee intervenes or interacts with living individuals for the purpose of research, obtains individually identifiable private information about living individuals for the purposes of research, or receives an award to conduct human research even when all activities involving human participants are carried out by a subcontractor or collaborator.⁹ This includes all human subject research that is:
1. Sponsored by any of the institutions subject to this Policy; or
 2. Conducted by or under the direction of any employee (including faculty or staff), agent, student, fellow, or post-doctoral appointee of WU/BJH/SLCH in connection with his/her institutional responsibilities, employment or academic status; or
 3. Conducted in accordance with an assurance filed with OHRP in which WU is designated as the IRB of record.
 4. Theses and dissertations prepared by WU students to meet the requirements of an advanced degree are expected to meet the regulatory definition of “research” as defined in Section II(F)(1) of this Policy, and require HRPO review and approval if the HHS definition of “human subject” is also met.
 5. Honors theses or projects prepared by WU undergraduate students to meet graduation requirements for Latin honors are considered original work, are citable, and are expected to otherwise meet the federal regulatory definition of “research” as defined in Section II(F)(1) of this Policy and require IRB review and approval if the federal definition of “human participant” as defined in Section II(F)(1) is also met.
- B. In the conduct of non-exempt cooperative research, each institution is responsible for safeguarding the rights and welfare of human participants and for complying with the Common Rule. “Cooperative research projects” are projects covered by this policy which involve more than one institution. When a cooperative agreement exists, the WU IRB may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.¹⁰ When doing so, the HRPO will ensure that:
1. The review arrangement is approved, in writing, by the appropriate officials of the institutions involved, and
 2. When WU IRB has been designated the IRB of record, the particular characteristics of the local research context are considered either (i) through knowledge of the local research context by the WU IRB or (ii) through subsequent review by appropriate designated WU officials, such as the Executive Chair and/or other WU IRB members, or an external consultant.¹¹
- C. The WU IRB has designated the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) ([IRB00000781](#)) and Pediatric Central Institutional Review Board (PCIRB) ([IRB00004296](#)) as the IRB of record for applicable NCI Cooperative Group studies. The WU IRB will perform local institution functions and will rely on the NCI CIRB and PCIRB to fulfill their stated responsibilities, as outlined for both in the “Division of Responsibilities between

NCI's Central IRB and Participating Local Institutions"
(www.ncicirb.org/Div_Responsibilities1.pdf).

- D. When WU is the coordinating center and/or the WU PI/PD is the lead investigator for multi-center research, the WU PI/PD must ensure that IRB approval has been obtained at each participating site prior to initiation of the research at that site. Copies of the non-WU site's IRB approval must be provided to the WU IRB. The IRB will assess the procedures for dissemination of protocol information (e.g. unanticipated problems involving risks to participants or others, modifications, interim findings) to all participating sites.
- E. When an external organization or facility acts as a performance site only and is not engaged in research, the PI must obtain a written letter of permission from an authorized representative of the organization or facility acknowledging their agreement to serve as a site for the research activities. A copy of this letter of permission must be provided to the IRB. Email correspondence is considered an adequate method for obtaining permission. The date of the permission letter must be prior to the start of the data collection at the site.
- F. The IRB will review research under its jurisdiction, as described in Section II(A). above, to determine whether the research activities meet one or more of the exempt categories allowed by federal regulations. Only the IRB has the authority to determine if the proposed research activities qualify as exempt. Research will be determined to be exempt only when the sole involvement of human participants will be in one or more of the categories listed in 45 CFR 46.101(b)(1-6), or, in the case of FDA-regulated research, 21 CFR 56.104 or exempted under WU's Category 2a exemption (as defined in the glossary).
 - 1. Research conducted under exempt review is subject to all applicable WU institutional and IRB policies and procedures.
 - 2. Any proposed changes to research determined by the IRB to be exempt must be submitted for review and approval prior to implementation. The IRB review will ensure that the research continues to be conducted ethically and that the research continues to meet the requirements for exemption.
 - 3. The IRB will not consider any research exempt that involves:
 - a. greater than minimal risk
 - b. prisoners;
 - c. observation of behavior that takes place in settings where participants have a reasonable expectation of privacy;
 - d. deception of research participants;
 - e. research that involves a test article regulated by the FDA unless the research meets the criteria for exemption described in 21 CFR 56.104; and
 - f. use of a medical device on specimens (including case and control specimens).¹²
 - 4. The Executive Chair or designated committee member will review the proposed research and will validate or decline the investigator's claim for exemption, ensure that risks to individuals are minimized, and confirm that the research meets ethical standards, such as equitable participant selection, provisions to maintain the confidentiality of data and privacy interests of participants, and the requirement of a consent process if there are interactions with the participants. The IRB will document in the protocol file

the review and determination of the Executive Chair or designee including the category specified in 45 CFR 46.101(b) (1-6) or, in the case of FDA-regulated research, 21 CFR 56.104 or WU's Category 2a exemption, justifying the classification of exempt.

5. The IRB will promptly notify the PI/PD in writing of its decision regarding the research. If it is determined that the research is not exempt or if modifications are required such as submission of a consent document or strengthening of protections in place to minimize risks to participants, the IRB will include in its written notification a statement of the reason for its decision and give the PI/PD an opportunity to respond in person or in writing. Final approval of exempt research will be made pending resolution of all contingencies identified by the reviewer.
6. If the IRB determines that the proposed research does not meet the criteria for exemption, the PI/PD must submit a new application for the appropriate method of review (expedited or full board) unless the exempt submission provides sufficient information for consideration by the expedited reviewer or the full board.
7. At the time of approval of exempt research, PI/PDs are reminded of their responsibility to submit modifications and unanticipated problems involving risks to participants or others in accordance with Section VI(C) and (E) of this policy.
8. Applications for exempt research are reviewed in the same manner as expedited protocols, as described in Section VI of this Policy. All determinations made by the Executive Chair, or designee, regarding exemptions are reported to a full board committee.
9. Institutional policy prohibits the conduct of "Classified" research at WU.¹³

G. Definitions of Human Research

"Human research" is defined as any activity that represents "research" involving "human participants" defined by HHS regulations or a "clinical investigation" of a "test article" involving one or more "human participants" as defined by FDA regulations as follows.

1. HHS Definitions

- a. *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. [45 CFR 46.102(d)]
- b. *Human participant* means a living individual about whom an investigator (whether professional or student) conducting research obtains (i) data through intervention or interaction with the individual, or (ii) identifiable private information. *Intervention* includes both physical procedures by which data are gathered and manipulations of the participant or the participant'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. Private information must be individually identifiable (i.e., the identity of the participant 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)]

2. FDA Definitions

- a. *Clinical investigation* means any experiment that involves a test article and one or more *human participants* and that is one of the following: [21 CFR 50.3(c)] [21 CFR 56.102(c)]
 - i. subject to requirements for prior submission to the FDA under §505(i) or §520(g) of the (FDA) act; or
 - ii. not subject to requirements for prior submission to the FDA under these sections of the (FDA) act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
- b. The term clinical investigation does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies.
- c. *Human participant* means an individual who is or becomes a participant in research, either as a recipient of a *test article* or as a control or an individual on whose specimen a medical device is used. A participant may be either a healthy human or a patient. [21 CFR 50.3(g)]
- d. *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act. [21 CFR 50.3(j)] [21 CFR 56.102(l)]

H. Determinations of the Conduct of Human Research.

1. Investigators are expected to recognize when they are engaged in activities subject to IRB jurisdiction by complying with this Policy and other relevant institutional policies and procedures. If uncertain, an investigator may submit a written request to the IRB for a determination.
2. Applications for human research determinations will be reviewed according to the Expedited Review procedures described in Section VI(A)(1) of this Policy. Determinations will be based on whether the activity meets the definitions of “human research” as outlined in Section II(G) of this Policy.
3. Determinations will be communicated to investigators in writing, a copy of which will be retained by the HRPO.
4. Changes in activity(ies) previously determined by IRB as not human research may be submitted for a determination of whether the change(s) continue to represent activities that are not human research.
5. When the research method involves obtaining coded private information or specimens, the IRB will review the research according to parameters described in OHRP *Guidance on Research Involving Coded Private Information or Biological Specimens*. Activities that do not involve human participants, according to the current *Guidance*, will be designated as such. Only the IRB has authority to determine that research involving coded private information or specimens does not involve human participants.
6. If an investigator begins a non-research project that involves human participants and later finds that the data gathered could contribute to generalizable knowledge, the investigator must submit a proposal to the

IRB for review and approval prior to using the data to develop the publication or presentation of the data (e.g., journal article, poster session, public speech, or presentation).

- I. Failure to Submit a Project for IRB Review
 1. The implications of engaging in activities that qualify as human research that is subject to IRB review without obtaining such review are significant. Results from such studies may not be published or presented unless IRB approval has been obtained prior to collecting the data. To do so would be in violation of this Policy. Similarly, human research data collected to satisfy thesis or dissertation requirements without prior IRB approval is a violation of this Policy.
 2. If an investigator begins a project and later finds that the data could contribute to generalizable knowledge the investigator must submit a proposal to the IRB for review and approval prior to release of the data.
 3. The IRB will not approve applications in which the investigator has attempted to circumvent IRB policies and procedures regarding human research by collecting data as non-human research and then submitting them as existing data. It is therefore in the investigator's best interest to carefully consider the likelihood that the data will be used for research purposes in the future, and to err on the side of inclusion and seek IRB approval prior to commencing the work.
 4. Violations of this Subsection I may be considered serious or continuing non-compliance and will be handled according to the procedures described in Section X of this Policy.

III. Records

- A. The HRPO will prepare and maintain adequate documentation of IRB activities, including the following:
1. Protocol:¹⁴ All available and applicable documents related to submission of a research protocol including, but not limited to, the application, protocol, scientific evaluations, grant, Investigator's Brochure, consent form(s) (including approved sample consent documents for HHS funded protocols, if applicable), progress reports submitted by the PI/PD, recruitment and advertisement materials, study tools and instruments, reports of unanticipated problems involving risks to participants or others, and reports of injuries to participants.
 2. Minutes¹⁵
 - a. Minutes of the committee meetings document:
 - i. Attendance at meetings (including when an alternate member replaces a primary member)
 - ii. Actions taken by the Committee
 - iii. Separate deliberations for each action and the vote on these actions (including the number of members voting for, opposed, and abstaining). The vote will reflect only those present. Any member who recuses him/herself, due to a conflict will be noted by name in the voting record.
 - iv. Basis for requiring modifications or disapproving the research, and a summary of controverted issues and their resolution.
 - v. Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the HHS-approved sample consent document.
 - vi. The approval period for continuing review.
 - vii. Required regulatory determinations and protocol-specific findings justifying determinations for:
 - A. Waiver or alteration of the consent process
 - B. Research involving pregnant women, fetuses, and neonates
 - C. Research involving prisoners
 - D. Research involving children
 - E. The rationale for significant risk/non-significant risk device determinations.
 - b. Minutes are distributed to the Chair of the meeting and to Committee members (via email). Approval of the minutes by the Chair and the Committee members is indicated by their absence of response within five days of the request for comments.
 - c. Modifications of full board minutes that occur after committee approval will be communicated to members via email distribution of an addendum to the minutes. Approval of the addendum by the Committee members is indicated by their absence of response within five days of the request for comments.
 3. Continuing Review:¹⁶ Records of Continuing Review activities including, but not limited to, the continuing review application, the most current protocol, updated consent form(s), progress report (if funded by a granting agency and available), data monitoring reports (if applicable), study tools and instruments, recruitment and advertising materials, and an aggregate listing of reported unanticipated problems involving risks to participants or others and other reportable events as required by this policy.

4. Correspondence: Copies of all relevant correspondence between the IRB, and PI/PDs will be filed in the relevant protocol file.
 5. Membership Lists¹⁷
 - a. A list of Committee members which includes demographic information and area of expertise, as applicable
 - b. All changes in Committee membership will be reported by the Operations Manger to OHRP quarterly (as requested by OHRP).
 6. Policies and Procedures:¹⁸ Written procedures which the IRB will follow for:
 - a. Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution (See Sections V and VI of this Policy);
 - b. Determining which protocols require review more often than annually and which protocols need verification from sources other than the investigators that no material changes have occurred since previous IRB review (See Sections V(B)(8) and IX(O) of this Policy);
 - c. Ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the participant (See Sections VI(C) and IX(E) of this Policy); and
 - d. Ensuring prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of (i) any unanticipated problems involving risks to participants or others, (ii) any serious or continuing noncompliance with this Policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval (see Section X of this Policy).
 7. New Findings: Statements that the PI/PD will inform the participants of significant new findings developed during the course of the research which may affect the participant's willingness to continue participation (See Sections V(D), VI(C) and X of this Policy).
 8. Budget and Accounting Records: Budgets are prepared on an annual basis by the HRPO.
 - a. School of Medicine: Resource allocations are determined based on cost analysis of expenses in the prior fiscal year and comparison to fair market value for salaries and equipment. The HRPO identifies necessary resources and factors these expenses into the budget proposed to the Dean of the Medical School.
 - b. Danforth Campus: Annual budget is approved by the Central Fiscal Unit.
 9. Emergency Use Reports: All documents related to Emergency Use of an FDA-regulated test article including, but not limited to, the IRB application, protocol and Investigator's Brochure (if available), and consent form.
- B. The above administrative records and records relating to research will be retained by the IRB for a minimum of 7 years after the research is completed, for a minimum of 7 years if the research is cancelled without participant enrollment, or longer as required by law.
- C. All records are accessible for inspection and copying by authorized representatives of HHS, FDA, representatives of federal funding agencies,

Industry Sponsors, and WU officials and internal auditors at reasonable times and in a reasonable manner.¹⁹

IV. Membership/Committees

- A. The WU FWA designates 11 full board reviewing committees. Of these committees, the Protocol Adherence Review Committee (PARC), reviews issues that may represent serious or continuing noncompliance. Each committee meets once monthly and/or on an ad hoc basis. Membership lists are on file in the HRPO office and at the OHRP. Each committee member is charged with ensuring the protection of the welfare and safety of research participants by assuring that WU researchers adhere to ethical, regulatory, and Institutional requirements.
- B. Committee Make-up:²⁰ Each Committee:
1. Is comprised of at least five members (on average 15-25 members) with varying backgrounds and expertise to promote complete and adequate review of research activities commonly conducted by the Institution.
 2. Is qualified through the experience and expertise of its members.
 3. Is qualified through the diversity of its members including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes. None of the WU Committees consist of entirely men, women, or members of one profession.
 4. Is competent to review specific research activities and able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.
 5. Includes at least one member whose primary concerns are in a scientific area, at least one member whose primary concerns are in a non-scientific area and at least one member who is not otherwise affiliated with the Institution and who is not part of the immediate family of a person who is affiliated with the Institution.
- C. If the IRB is reviewing research involving a population vulnerable to coercion or undue influence, including but not limited to, prisoners, children, pregnant women, cognitively or decisionally-impaired, and economically or educationally disadvantaged, the IRB will ensure that the protocol is reviewed by one or more individuals who are familiar with the population. The IRB will regularly examine its local research context for other vulnerable populations that should be represented to ensure that the research is reviewed by an IRB member or consultant who is knowledgeable about or experienced in working with that population. The review of initial and continuing review of research, modifications of research and unanticipated problems involving risks to participants or others involving prisoners will include review by a prisoner representative to confirm that the research meets or continues to meet the regulatory criteria for inclusion of prisoners.²¹
- D. Conflicts of Interest
1. No IRB member may participate in the review of any protocol in which he or she has a conflicting interest, except to provide information requested by the IRB. Members are expected to self-identify conflicting interests. A primary reviewer or expedited reviewer with a conflict of interest must notify the HRPO staff who will re-assign the protocol.

2. Conflicting interests include both financial and non-financial interests (as defined in the Glossary) which might interfere with the review process either by competing with an IRB member's obligation to protect participants or by compromising the credibility of the research review process.
 3. Except when requested to be present to provide information, IRB members will recuse themselves from the meeting room when research in which they have a conflicting interest is reviewed.
 4. The Chair will allow for committee discussion once the conflicted individual has left the meeting room. Any absent member is not counted toward quorum and his/her absence during the discussion and vote on the protocol will be noted in the IRB meeting minutes as being absent due to a conflict of interest.²²
 5. The IRB will maintain documentation that all members are aware of and committed to compliance with the IRB policy regarding conflicts of interest.
 6. When a Chair recuses him/herself due to a conflict, either the identified Vice Chair or the HRPO administrative representative, will serve as Chair.
- E. When necessary, the IRB may invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. Individuals who have a conflict of interest as defined in IRB policies cannot act as a consultant for any review. Consultants will be asked to sign the HRPO Assurance on Conflict of Interest and Professional Conduct to document that they do not have a conflict of interest for each review in which they participate. The signed assurance will be included in the study file.
1. Full Board Review: The need for a consultant may be identified prior to the review by a fully convened committee or requested by the committee during the review. The Full Board Analyst will initiate contact with the proposed consultant.
 - a. If identified prior to the meeting the Full Board Analyst will work in conjunction with the Full Board Manager to identify and contact an individual with appropriate expertise.
 - b. If requested by the committee, the committee will recommend an appropriate individual or the Full Board Analyst in conjunction the Full Board Manager will identify the appropriate individual.
 - c. The consultant's findings will be presented to the committee for consideration either in person, by a member of the board or by the HRPO staff. If in attendance, these individuals will provide consultation but will not participate in or observe the vote.²³ Information provided by consultants is documented in the meeting minutes.
 - d. Ad hoc or informal consultations requested by individual members (rather than the full board) will be requested in a manner that protects the researcher's confidentiality and is in compliance with the IRB conflict of interest policy (unless the question raised is generic enough to protect the identity of the particular PI/PD and research protocol).
 2. Expedited Review: Consultants will be approached by the expedited reviewer to provide an expert review of an entire protocol or a specific issue associated with a protocol. Information provided by consultants is documented in the study file.

- F. Non-members attending meetings will sign the HRPO Assurance on Conflict of Interest and Professional Conduct. Attending non-members will recuse themselves from the meeting room when the IRB reviews research in which they have a conflicting interest. This will be noted in the IRB meeting minutes.
- G. Recruitment and Conditions of Membership
1. IRB members are sought through recommendation from Deans and Department Heads, recommendations from other IRB members, or on a volunteer basis. IRB members and alternates are appointed by Executive Chair and Executive Director for an unlimited term.²⁴ IRB members may be recommended but are not selected by Investigators and Investigators may not specify which members review their submissions.
 2. IRB members serve as volunteers (without payment) except for the Executive Chair (whose salary is partially reimbursed by the Executive Vice Chancellor and Dean), the Chair of the Behavioral subcommittee (whose salary is partially reimbursed by the Executive Vice Chancellor for Administration and Finance) and HRPO staff members that also serve as IRB committee members.
 3. Committee members are covered by the WU self-insured liability program except for gross, intentional non-compliance with the IRB's mission.²⁵
 4. IRB members designated as alternates may represent the primary member in their absence and are included on the membership lists on file at the OHRP. Meeting minutes will document when an alternate attends a meeting for a committee member. If an alternate chooses to attend a meeting at which the committee member is present, the alternate's vote will not be counted and their presence will not count towards quorum.
 5. The Executive Chair is responsible for periodic evaluation of the performance of IRB members (including Chairs) and for the periodic evaluation of committee composition to confirm adherence to regulatory and institutional requirements. The HRPO conducts annual committee member surveys to evaluate member satisfaction and identify continuing education topics.
 6. Each IRB member will serve an initial three year appointment. Following initial appointment and at the time of annual evaluation, upon mutual agreement of the member and the Executive Chair the IRB member may be reappointed for additional one year term(s). An IRB member may be considered for removal from membership if he/she is not acting in accordance with the IRB's mission or policies and procedures after consultation with the Executive Chair of the IRB and the Executive Director of HRPO.
 7. Chairs are selected on the basis of their institutional commitment, knowledge of research and regulatory affairs, personal integrity, and ability to conduct an effective meeting.
 8. Each Chair has a Vice Chair who will chair the committee meeting in his/her absence. In instances when both the Chair and the Vice Chair are unable to attend the committee meeting, the Executive Chair or the HRPO management will identify a qualified member of the committee to chair the meeting.
- H. Full Board Committee Member Education (for the purposes of this Policy, the term "members" includes Chairs)

1. New IRB members are required to attend an introductory training session and observe at least one committee meeting prior to formally receiving protocols and voting at a committee meeting.
 - a. Training sessions focus on educating members in the responsibilities and obligations of committee members regarding the protection of human participants, applicable federal regulations and guidance documents, local IRB requirements, and on the regulatory requirements for approval of new and continuing review of human research.
 - b. Reference materials available to new members on the HRPO website include “The Belmont Report”, 45 CFR 46, 21 CFR 50, 21 CFR 56, the OHRP Guidebook and FDA Information Sheets and the HRPO forms and guidelines. New members also receive a copy of Robert Amdur and Elizabeth Bankert’s *Institutional Review Board Member Handbook: Second Edition*.
2. All IRB members must meet the HRPO education requirement by completing the designated CITI modules (located at <https://aisinfo.wustl.edu/ra.html>).
3. Ongoing education for members includes educational materials in meeting packets; HRPO Question and Answer sessions (held bimonthly); HRPO lectures, educational sessions, or retreats held throughout the year; and other local, regional, or national meetings when appropriate. A current listing of educational opportunities is published on the HRPO website (<http://hrpo.wustl.edu>).
4. When possible, the HRPO will fund committee members’ and/or Chairs’ attendance at regional or national conferences.
5. The HRPO has a library of human participant-related books, videotapes, and audiotapes available for checkout by committee members and the WU/BJH/SLCH research community. In addition, the HRPO maintains a computer-based library of related information.

V. Full Board Review

A. Convened Meetings

1. All protocols that do not qualify as exempt or allow for review by expedited procedure will be reviewed by a fully convened committee. Submissions that do not qualify for review by expedited procedure will be individually presented, discussed, and voted on at a convened meeting.
2. Full Board review of protocols will take place only when a quorum is achieved. Quorum is defined as a majority (more than 50% of the full committee) of the Committee members present, including at least one member whose primary concerns are in nonscientific areas. No official actions will be taken at a meeting where a majority of the members, including a non-scientist, are not present.²⁶ If quorum is lost during a meeting, no official actions are taken until quorum is restored.
3. Full Board review of protocols involving FDA-regulated articles will only take place when at least one physician or pharmacist member is present.²⁷
4. IRB meetings will take place with all participating members physically present unless circumstances warrant conducting an IRB meeting via telephone conference call or using speakerphone.
 - a. Telephone conference call: Official actions may be taken at a meeting in which members participate via telephone when each participating IRB member (i) has received all pertinent material prior to the meeting, and (ii) can actively and equally participate in the discussion of all protocols (e.g. each member can hear and be heard by all other participating members). Satisfaction of these two conditions in addition to the standard regulatory requirements will be documented in the meeting minutes.²⁸
 - b. Speakerphone: If a member is not able to be physically present during a convened meeting but is available by telephone, the meeting can be convened using speakerphone. The member who is not physically present will be connected to the rest of the members via speakerphone so that all members will be able to discuss the protocol. Members participating by speakerphone may vote provided they have had an opportunity to review all of the materials the other members have reviewed.
5. All members' votes will be deemed equal and no proxy votes (written or by telephone) will be considered.²⁹

B. Full Board Review and Actions

1. Approval of a protocol at a committee meeting requires the approval of a majority of those members who are present at the meeting.
2. The committee's decision regarding approvability of new research, continuation of ongoing research, and modifications to previously approved research is based on satisfaction of the regulatory criteria outlined by HHS in 45 CFR 46.111(a)(1-7) and, when applicable, FDA in 21 CFR 56.111(a)(1-7).
3. In general, materials are made available (in either paper or electronic format) to committee members five to seven days in advance of the meeting to allow adequate time for review. Urgent review procedures may be invoked only under unusual circumstances. This does not include urgency that is a result of negligence or delay on the part of the investigator or his/her staff to submit human subjects applications in a timely fashion. However, the IRB does recognize that an investigator may be faced with an immediate deadline

- beyond his or her control. The materials are distributed as soon as possible to committee members to allow sufficient time for review prior to the meeting.
4. The IRB will review all protocols for scientific or scholarly validity. This review is accomplished by the scientist members of the committee. IRB review also considers the presentation of supporting background scientific information including animal studies (whenever applicable). Scientific design or scholarly validity is considered an important criterion of approvability and is examined in relationship to the risk and benefits of the research. In addition, the signature of the Dean/Department Head (or designee) documents that a scientific or scholarly review has been conducted, the PI/PD is qualified to conduct the research and adequate resources are available for conduct of the research.
 5. The IRB will review all new project applications and continuing review applications to determine the appropriateness of the research in the local research context. Review and approval will be based on detailed applicable information provided in the application (e.g. participant population, participant selection, benefits to participants, mechanisms for protecting privacy, method for minimizing the possibility of coercion, etc.).
 6. The IRB may make one of the following determinations as a result of a full board review. In all instances, the approval date is the date of the convened meeting at which the committee confirmed that the criteria for approval were met. The expiration date will be within one year of the approval date and represents the last date that the protocol is approved.
 - a. Approval: The protocol and accompanying documents are approved as submitted.
 - b. Approved pending: The protocol and accompanying documents are approved pending review and acceptance of the stated contingencies by the IRB Chair or by an individual designated by the IRB.
 - c. Tabled: The committee determines that the Investigator's responses be reported back to its next convened meeting.³⁰ The protocol and accompanying documents cannot be approved without a response from the PI/PD and subsequent reconsideration, discussion, and vote by the committee. When the committee requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly relevant to the determinations required by 45 CFR 46.111 and 21 CFR 56.111, approval will be deferred pending subsequent review of the PI/PD's responses by committee.
 - d. Disapprove: The protocol fails to meet one or more of the criteria for approval.
 7. The IRB will promptly notify the PI/PD in writing (via email) of its decision to approve, disapprove, or require modifications to proposed research. If the IRB decides to disapprove a research activity, it will include in its written notification a statement of the reasons for its decision and give the PI/PD an opportunity to respond in person or in writing. The PI/PD is responsible for communicating the IRB decision to the Sponsor of the research (if applicable).
 8. At the time of initial review and at continuing review, the committee will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year for the duration of the research (including when study activity is limited to long-term follow-up of participants,

even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions and/or remaining activities that involve collection or analysis of identifiable data). In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of participants) may be required. The determination regarding the appropriate review intervals will be made based on considerations of the potential or actual risks of the research, the degree of novelty of the research intervention, the number of participants to be enrolled, any specific vulnerability associated with the research population, and/or the magnitude or frequency of risk to participants. The meeting minutes will reflect the committee's determination regarding review frequency.³¹

9. At the time of initial and continuing review, the committee will make a determination regarding the risks associated with the research protocols. The meeting minutes will reflect the committee's determination regarding risk levels. Research with adult populations will be classified as either "minimal" or "greater than minimal" based on the "absolute" interpretation of minimal risk as defined in 45 CFR 46.102(i). Risk assessment in research involving children as participants will be determined according to the requirements in 45 CFR 46.404-406. See Section VIII(C) for additional requirements on research involving children participants. The meeting minutes or the reviewer sheets will reflect the committee's determination regarding risk levels.
10. Full Board review of modifications to previously approved research, unanticipated problems involving risk to participants or others, and new information that may affect the participant's willingness to participate or continue participation in the study
 - a. The PI/PD must submit sufficiently detailed updated materials regarding the research in order for the committee to determine:
 - i. whether the proposed research continues to meet the requirements outlined in 45 CFR 46.111 and 21 CFR 56.111,
 - ii. that any significant new findings that arise from the review process and that may relate to participants' willingness to continue participation will be provided to participants.
 - b. The HRPO assigns one or two primary reviewers to each modification, unanticipated problem or report of new information. The Primary reviewer(s) will be assigned based on related expertise. When making reviewer assignments, the HRPO staff will take into consideration the vulnerable populations involved in the research and ensure at least one individual who has experience with this population is scheduled to be present at the meeting. The primary reviewer(s) are responsible for conducting an in-depth review of all submitted materials and presenting the research to the committee. All members (including alternate members) are expected to review materials in enough depth to discuss the information when they are present at the convened meeting. Materials provided to all committee members include:
 - i. The revised application and/or the report of the unanticipated problem or new information and any supporting documents (i.e. revised protocol, revised consent form)
 - ii. Current consent document

- iii. When applicable, a copy of the most recent continuing review information or the initial IRB application if the protocol has been open less than a year.
 - iv. A copy of the expedited reviewer's comments, if the protocol has been referred from expedited review.
 - c. Protocol expiration: The protocol expiration date remains unchanged after approval of a modification, unanticipated problem, or report new information unless otherwise voted upon and approved by the convened IRB.
- C. Full Board Review of New Protocol Submissions
1. In order for the committee to determine whether the proposed research meets the requirements outlined in 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7), the PI/PD must submit sufficiently detailed materials regarding the research.
 2. Primary Reviewers:³² The HRPO will assign one or two primary reviewers to each protocol. The Primary reviewer(s) will be assigned protocols based on related expertise. When making reviewer assignments, the HRPO staff will take into consideration the vulnerable populations involved in the research and ensure at least one individual who has experience with this population is scheduled to be present at the meeting. Primary reviewers are responsible for conducting an in-depth review of all pertinent documentation (see below) and presenting the research at the convened committee meeting. Materials provided to primary reviewers are:
 - a. Complete application including the signature of the PI/PD documenting his/her agreement to adhere to the information listed on the Assurances document and the signature of the Department Head (or designee) documenting that a scientific or scholarly review has been conducted;
 - b. Approximate number of subjects to be accrued at Washington University and group wide (when applicable).
 - i. Open-ended enrollment is not allowed.
 - ii. The estimate is used as a guide and compared to the number of participants actually accrued which is reviewed at the time of continuing review.
 - iii. If the number of anticipated participants to be accrued needs to be altered, a modification should be submitted..
 - c. Full protocol;³³
 - d. Proposed informed consent document(s);
 - e. A copy of the HHS-approved informed consent document and the complete HHS-approved protocol when they exist.
 - f. Relevant grant application (The protocol and grant application should be in full concordance.);
 - g. Investigator's Brochure (if one exists);
 - h. Copies of surveys, questionnaires, study tools, or instruments;
 - i. Recruitment materials and advertisements intended to be seen or heard by potential participants.
 - j. Documents pertaining to scientific reviews conducted by WU ancillary committees (when applicable);
 - k. A copy of the expedited reviewer's comments (when applicable); and
 3. All other committee members receive the application form (which includes a protocol summary sufficient to make the determinations required under 45

CFR 46.111 and 21 CFR 56.111), the proposed informed consent document(s), and any recruitment materials or advertisements intended to be seen or heard by potential participants. Complete documentation is available to all members for review at or prior to the convened meeting.³⁴ All members (including alternate members) are expected to review materials in enough depth to discuss the information when they are present at the committee meeting.

4. Review of recruitment materials/advertisements and participation payments: Advertising and recruitment is the start of the informed consent and participant selection process. The IRB will review the advertisement as well as the mode of communication to assure that it is not coercive or unduly influential and does not promise a benefit beyond what is outlined in the consent and the protocol. The IRB will promptly notify the PI/PD in writing of its decision regarding the proposed recruitment materials or advertisements.
 - a. The IRB will review all recruitment materials to ensure that the advertisement is limited to the information the prospective participants need to determine their eligibility and interest. When appropriate, the following items may be (but are not required to be) included in advertisements:
 - i. the name and address of the PI/PD and/or research facility;
 - ii. the condition under study and/or the purpose of the research;
 - iii. in summary form, the criteria that will be used to determine eligibility for the study;
 - iv. a brief list of potential participation benefits, if any;
 - v. the time or other commitment required of the participants; and
 - vi. the location of the research and the person or office to contact for further information.³⁵
 - b. The IRB must review direct advertising for research participants (i.e., advertising that is intended to be seen or heard by prospective participants to solicit their participation in a study) but does not need to review news stories or publicity intended for other audiences (such as financial page advertisements directed toward prospective investors).
 - c. IRB review of listings of clinical trials on the internet is not required when the system format limits the information provided to basic trial information, such as: the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information. If the system format includes additional descriptive information, IRB review and approval is required to ensure that the additional information does not promise or imply a benefit beyond what is contained in the protocol and the consent document.
 - d. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects.
 - e. The IRB must review the final audio/video tapes for broadcast. In these instances, the IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording.
 - f. Advertisements should not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol
 - i. No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under

- investigation, that the test article is known to be equivalent or superior to any other drug, biologic or device, or that is otherwise inconsistent with FDA labeling.
- ii. Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational.
- iii. Coupons good for a discount on the purchase price of a product once it has been approved for marketing are not allowed as compensation.
- g. Advertisements should not promise "free medical treatment," when the intent is only to say participants will not be charged for taking part in the investigation.
- h. Advertisements may state that participants will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.
- i. The IRB must review the amount, proposed method, and timing of any payment to participants to ensure that:
 - i. payment is neither coercive nor presents undue influence;
 - ii. Credit for payment accrues as the study progresses and is not contingent on completion of the entire study; and
 - iii. Any bonus payment for completion of the study is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
- j. All information concerning participant payment including the amount and schedule is described in the informed consent document.

D. Continuing Review by the Full Board

1. The PI/PD must submit sufficiently detailed updated materials regarding the research in order for the committee to determine:
 - a. whether the proposed research continues to meet the requirements outlined in 45 CFR 46.111 and 21 CFR 56.111,
 - b. the protocols that need verification from sources other than the investigators that no material changes had occurred since the previous IRB review,
 - c. that the current consent document is still accurate and complete, and
 - d. that any significant new findings that arise from the review process and that may relate to participants' willingness to continue participation will be provided to participants.
2. Primary Reviewers:³⁶ The HRPO will assign one or two primary reviewers to each "Greater than Minimal" risk protocol renewal. The Primary reviewer(s) will be assigned protocols based on related expertise. When making reviewer assignments, HRPO staff will take into consideration the vulnerable populations involved in the research and ensure that at least one individual who has experience with this population is scheduled to be present at the meeting. The primary reviewer(s) are responsible for conducting an in-depth review of all pertinent documentation (see below) and presenting the research to the committee. Materials provided to the primary reviewer(s):
 - a. Complete continuing review application which includes:
 - i. Protocol summary;
 - ii. Status report on the progress of the research;
 - iii. Number of participants accrued;

- iv. Summary of any adverse events or unanticipated problems involving risks to participants or others, withdrawal of participants from the research and the reasons for withdrawals, and complaints about the research since the last IRB review;
 - v. Most recent data/safety monitoring report (when applicable);
 - vi. Summary of any relevant recent literature, findings obtained thus far, modifications to the research since the last IRB review, any relevant multi-center trial reports;
 - vii. Any other relevant information (especially information about risks associated with the research); and
- b. Complete protocol including any modifications previously approved by the IRB;³⁷
 - c. Granting agency progress report, if applicable and available (The grant progress report or any changes as a result of competitive renewal will be reviewed for concordance with the protocol.);
 - d. A copy of the current consent document(s) and any newly proposed consent document (If the protocol is closed to accrual but participants continue to receive treatment, the IRB will review the most current approved consent form with the renewal.) If there are proposed changes to the consent form, such changes will be highlighted in the revised version of the consent form;
 - e. Recruitment materials and advertisements intended to be seen or heard by potential participants that are being revised or added at the time of IRB review;
 - f. Documents pertaining to scientific reviews conducted by WU ancillary committees (when applicable) and;
 - g. If modifications are submitted at the time of continuing review, a revised application and any revised and/or supporting documents
3. All other Committee members receive the application form (the specifics of which are outlined above), a copy of the current consent document(s), and any newly proposed consent document with any changes highlighted. Complete documentation (including the protocol file) and relevant IRB minutes are available to all members for review upon request. All members (including alternate members) are expected to review materials in enough depth to discuss the information when they are present at the convened meeting.
 4. All continuing review submissions that do not qualify for review by expedited procedure will be individually presented, discussed, and voted on at a fully convened committee meeting.
 5. All continuing reviews that meet the criteria required in Categories 8 or 9 of the list of research activities which may be reviewed through expedited review procedures (63 FR 60364-60367), will be reviewed by qualified members who have been designated by the Executive Chair to conduct expedited review. All expedited reviews of protocols will be reported to the Full Board (see Section VI(B) of this Policy).
 6. Expiration of IRB Approval:³⁸ There is no grace period extending the conduct of research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted.
 - a. All research activity must stop and new participants cannot be enrolled.
 - b. Research interventions or interactions involving already enrolled participants may only continue with written documentation that the IRB

finds that it is in the best interest of the individual participants to do so and when the IRB has confirmed that the PI/PD is actively pursuing protocol renewal.³⁹

- c. When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval will not be reported to OHRP or the FDA as a suspension of IRB approval.⁴⁰

VI. Expedited Review

A. General Expedited Review

1. The Executive Chair designates IRB members to conduct expedited review in accordance with 45 CFR 46.110 and (when applicable) 21 CFR 56.110. Only research that meets the specific criteria outlined in “Research Activities Which May Be Reviewed Through Expedited Review Procedures” (63 FR 60353-60356 and 63 FR 60364-60367) will be reviewed by an expedited review process. Reviewers conducting expedited review are members of a full board committee, experienced as IRB members through appropriate training. Appropriate training includes, but is not limited to directed education by a HRPO Manager on expedited review policies and procedures.
2. Expedited reviewers review for scientific or scholarly validity, consistency with ethical principles, and compliance with federal regulations and University policies and procedures. The expedited reviewers meet with the Executive Chair, Executive Director or Behavioral Minimal Risk Chair as needed to discuss application of the expedited categories and specific protocols that require further evaluation.
3. Designated reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. The research may only be disapproved after review in accordance with the non-expedited review procedure set forth in 45 CFR 46.108(b) and 21 CFR 56.108(c).⁴¹ When applicable, contingencies will be communicated to the PI/PD in writing. If a PI/PD does not agree to make the reviewer’s requested revisions, research will be reviewed by a fully convened committee.
4. The IRB will employ the use of the expedited review mechanism only for minor modifications to ongoing research involving prisoners and continuing review of research involving prisoners that meets expedited categories 8(a), (b) or (c) as defined in HHS guidance, “Categories of Research That May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure” (63 FR 60364-67 11/9/98).” The prisoner representative will contribute to the expedited review to confirm that the request meets the criteria for expedited review and that the research continues to meet the regulatory criteria for inclusion of prisoners.
5. Requests for expedited review that, upon review, are determined not to meet the criteria for expedited review will be reviewed by fully convened committee (see Section V(A)(1) of this Policy).
6. The fully convened committees will be kept apprised of expedited approvals of initial, continuing review, and minor modifications to previously approved research.
 - a. Findings of determinations made by expedited review procedures are reported to a designated full board committee (03A).
 - b. See Sections VI (B)(1), (C)(1), (D)(1), and (E)(1) for a description of the expedited review process. Reports are available, in writing, at the time of the meeting.
7. The Executive Chair, WU officials, OHRP, or FDA may restrict, suspend, terminate, or choose not to authorize the IRB’s use of the expedited review procedure when necessary to protect the rights and welfare of participants.⁴²

8. Expedited reviewers are asked to self-identify conflicts of interest as defined in the Glossary and notify the HRPO staff if a conflict exists.
- B. Expedited review of new project applications and continuing review applications
1. The expedited reviewer conducts an in-depth review of the following materials (provided to reviewers at the time of review):
 - a. New application review:
 - i. Complete application including the signature of the PI/PD documenting his/her agreement to adhere to the information included in the Assurances document and the signature of the Dean/Department Head (or designee) documenting that a scientific or scholarly review has been conducted; the qualifications of the PI/PD and adequate resources are available for conduct of the research.
 - ii. Approximate number of subjects to be accrued at Washington University and group wide (when applicable).
 - A. Open-ended enrollment is not permitted.
 - B. The estimate is used as a guide and compared to the number of subjects actually accrued.
 - C. If the number of anticipated subjects to be accrued needs to be altered, IRB approval must be sought before enrolling additional participants/collecting data beyond the number approved by the IRB. A modification should be submitted for review and approval.
 - iii. Full protocol;
 - iv. Proposed informed consent document(s) or debriefing statement for undergraduate research (if applicable);
 - v. A copy of the HHS-approved informed consent document and the complete HHS-approved protocol when they exist.
 - vi. Relevant grant application(s) or progress reports (if applicable) (The protocol and grant application should be in full concordance.);
 - vii. Copies of surveys, questionnaires, study tools, or instruments;
 - viii. Recruitment materials and advertisements intended to be seen or heard by potential participants (if applicable)
 - ix. Documents pertaining to scientific reviews conducted by WU ancillary committees (when applicable)
 - b. Continuing Review:
 - i. Complete continuing review application;
 - ii. Status report on the progress of the research;
 - iii. Number of participants accrued;
 - iv. Summary of any adverse events or unanticipated problems involving risks to participants or others, withdrawal of participants from the research and the reasons for withdrawals, and complaints about the research since the last IRB review;
 - v. Most recent data/safety monitoring report (when applicable);
 - vi. Summary of any relevant recent literature, findings obtained thus far, modifications to the research since the last IRB review, any relevant multi-center trial reports;
 - vii. Any other relevant information (especially information about risks associated with the research);
 - viii. Complete protocol (may be a separate document or included in the information provided in continuing review application), including any modifications previously approved by the IRB;⁴³ The IRB may request

- a separate protocol document if sufficient detail is not provided in the continuing review application;
- ix. Informed consent document(s) or debriefing statement (If the protocol is closed to accrual but participants continue to receive treatment, the IRB will review the most current approved consent form with the renewal. If there are proposed changes to the consent form, all modifications will be highlighted in the revised version of the consent form.);
 - x. Granting agency progress report (if applicable); (The grant progress report or any changes as a result of competitive renewal will be reviewed for concordance with the protocol);
 - xi. Recruitment materials and advertisements intended to be seen or heard by potential participants that are being revised or added at the time of IRB review;
 - xii. Documents pertaining to scientific reviews conducted by WU ancillary committees (when applicable);
 - xiii. Study tools or instruments (when applicable); and
 - xiv. If modifications are submitted at the time of continuing review, a revised application and any revised and/or supporting documents
2. The reviewer will confirm and document in the protocol file that the research satisfies both the applicability criteria and specified expedited categories as required in HHS guidance, “Categories of Research That May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure” (63 FR 60364-67 11/9/98).” Reviewer(s) will document the specific permissible category or categories justifying the expedited review on the reviewer form.
 3. If the reviewer determines that the proposed research does not meet the criteria for expedited review, the submission will be reviewed by a fully convened committee (as described in Section V of this Policy).
 4. The reviewer’s decision regarding approvability of new research and continuation of ongoing research is based on satisfaction of all of the conditions outlined in 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7). At the time of continuing review the reviewer will also determine:
 - a. the protocols that need verification from sources other than the investigators that no material changes had occurred since previous IRB review;
 - b. that the current consent document is still accurate and complete, and
 - c. that any significant new findings that arise from the review process and that may relate to participants’ willingness to continue participation will be provided to participants.
 5. The reviewer will review all expedited protocols for scientific or scholarly validity. The reviewer will consider the presentation of supporting background scientific information including animal studies (whenever applicable). The protocol and grant application should be in full concordance.
 6. The reviewer may approve the research or require modifications to secure approval. If the reviewer can neither approve nor require modifications to secure approval, the research will be reviewed by a fully convened committee.
 7. The reviewer will document in the protocol file all determinations required by regulations and IRB policy including frequency of review and specific determinations for research involving children, prisoners, pregnant women

and fetuses, waivers and alteration of consent, and waivers of consent documentation.

8. The IRB will promptly notify the PI/PD in writing of its decision to approve, require modifications, or require full board review of the proposed research activity.
9. At the time of initial review and at continuing review, the expedited reviewer will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year for the duration of the research (including when study activity is limited to long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions and/or remaining activities that involve collection or analysis of identifiable data). In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of participants) may be required. The determination regarding the appropriate review intervals will be made based on considerations of the potential or actual risks of the research, the degree of novelty of the research intervention, the number of participants to be enrolled, any specific vulnerability associated with the research population, and/or the magnitude or frequency of risk to participants.⁴⁴
10. Expiration of IRB Approval:⁴⁵ There is no grace period extending the conduct of research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted.
 - a. All research activity must stop and new participants cannot be enrolled.
 - b. Research interventions or interactions involving already enrolled participants may only continue with written documentation that the IRB finds that it is in the best interest of the individual participants to do so and when the IRB has confirmed that the PI/PD is actively pursuing continuing review of the study.⁴⁶
 - c. When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval will not be reported to OHRP or the FDA as a suspension of IRB approval.⁴⁷

C. Review of changes in previously-approved research

1. Minor modifications in previously-approved research may be reviewed under expedited procedures. Expedited reviewers evaluate whether modifications represent a minor change. Minor modifications are defined as those that do not potentially adversely affect the overall assessment of the risks and benefits of the study and do not substantially change the specific aims/design of the study.
 - a. Examples of minor modifications include but are not limited to:
 - i. A minor increase or decrease in the number of participants. ;
 - ii. Adding or revising a study instrument or task condition;
 - iii. Small changes in remuneration;
 - iv. Changes to improve the clarity of statements or to correct typographical errors;
 - v. Change in research team members;
 - vi. Change in funding source; and
 - vii. Change in research performance (study) sites.

2. Review of proposed modifications that are not minor and/or do not qualify for an expedited category will be reviewed by a fully convened committee (see Section V(B)(10) of this Policy).
3. The PI/PD will submit a revised application, any supporting documents, and the revised documents (protocol, consent document, recruitment materials, questionnaires, etc.) for IRB review. The reviewer will conduct an in-depth review of this information.
4. The reviewer's decision regarding approvability of modifications to previously approved research is based on continued satisfaction of all the conditions outlined in 45 CFR 46.111(a)(1-7) and 21 CFR 56.111(a)(1-7). The reviewer will also determine that any significant new findings that arise from the review process and that may relate to participants' willingness to continue participation will be provided to participants.
5. When reviewing modifications to the consent document, the reviewers will take into consideration both prospective research participants and research participants already enrolled in the study. New findings developed during the course of the research which may affect a participant's willingness to continue participation must be provided to the participant in a letter of notification or by re-consenting the participant using a modified consent document. All such revised documents must be approved by the IRB..
6. The IRB will promptly notify the PI/PD in writing of its decision regarding the proposed modification.
7. Changes in approved research may be initiated without IRB approval only to eliminate apparent immediate hazards to the participant. These changes should be immediately reported after the occurrence. The events are reviewed by the IRB to determine whether the change was consistent with ensuring the participants' continued welfare. These events may require review by a fully convened committee if the change is considered to be more than minor.

D. Review of recruitment materials/advertisements and participation payments: Advertising and recruitment is the start of the informed consent and participant selection process. The IRB will review the advertisement as well as the mode of communication to assure that it is not unduly coercive, does not promise a benefit beyond what is outlined in the consent and the protocol, and does not include any exculpatory language. The IRB will promptly notify the PI/PD in writing of its decision regarding the proposed recruitment materials or advertisements.

1. The IRB will review all recruitment materials to ensure that advertisement to recruit participants is limited to the information the prospective participants need to determine their eligibility and interest. When appropriate, the following items may be (but are not required to be) included in advertisements:
 - a. the name and address of the PI/PD and/or research facility;
 - b. the condition under study and/or the purpose of the research;
 - c. in summary form, the criteria that will be used to determine eligibility for the study;
 - d. a brief list of potential participation benefits, if any;
 - e. the time or other commitment required of the participants; and
 - f. the location of the research and the person or office to contact for further information.⁴⁸

2. The IRB must review direct advertising for research participants (i.e., advertising that is intended to be seen or heard by prospective participants to solicit their participation in a study) but does not need to review news stories or publicity intended for other audiences (such as financial page advertisements directed toward prospective investors).
3. The IRB review and approval of listings of clinical trials on the internet is not required when the system format limits the information provided to basic trial information, such as: the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information. When the system format includes additional descriptive information, IRB review and approval is required to ensure that the additional information does not promise or imply a benefit beyond what is contained in the protocol and the consent document.
4. The IRB must review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects.
5. The IRB must review the final audio/video tapes for broadcast. In these instances, The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording.
6. Advertisements should not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol
7. No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation, that the test article is known to be equivalent or superior to any other drug, biologic or device, or that is otherwise inconsistent with FDA labeling.
8. Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational.
9. Coupons good for a discount on the purchase price of a product once it has been approved for marketing are not allowed as compensation.
10. Advertisements should not promise "free medical treatment," when the intent is only to say participants will not be charged for taking part in the investigation.
11. Advertisements may state that participants will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.
12. The IRB must review the amount, proposed method, and timing of any payment to participants to ensure that:
 - a. Payment is neither coercive nor presents undue influence;
 - b. Credit for payment accrues as the study progresses and is not contingent on completion of the entire study; and
 - c. Any bonus payment for completion of the study is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
13. All information concerning participant payment including the amount and schedule is described in the informed consent document.

VII. Informed Consent

A. General Consent Requirements⁴⁹

1. No PI/PD may involve a human being as a participant in research without obtaining the legally effective informed consent of the participant or the participant's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Section VII(B) of this Policy. In general, the IRB considers individuals who are unable to consent for procedures outside of the research context to be unable to consent for research participation. Tools or instruments such as the Mini Mental Exam can also be used to determine capability to consent.
2. Consent must always be sought under circumstances that:
 - a. provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate; and
 - b. minimize the possibility of coercion or undue influence.
3. The IRB will consider where the consent process will take place, timing of the consent process and the individual who will be obtaining consent (e.g. the PI/PD, collaborator, or qualified designee) in its determination regarding the appropriateness of the consent process. When the potential participant's understanding of the research may be impaired due to the timing, location, or individuals participating in the proposed consent process, the IRB will require an alternative process. (For example, the IRB may require that only the PI/PD or physician collaborator obtain consent or that consent be obtained prior to entry into the cardiac catheterization waiting area.)
4. The information that is given to the participant or the representative must be in language understandable to the participant or the representative. When a protocol includes a non-English speaking population, the consent form must be translated by a qualified translator to the participant's native language.
5. The IRB will not approve exculpatory language through which the participant or the representative is made to:
 - a. Waive or appear to waive any of the participant's legal rights; or
 - b. Release or appear to release to the PI/PD, the Sponsor, WU or its agents from liability or negligence.
6. In seeking informed consent the basic elements of informed consent (as stated in 45 CFR 46.116(a)(1-8)) and 21 CFR 50.25(a)(1-8) must be provided to each participant unless the IRB has approved an alteration of the basic elements (see Section VII(C) of this Policy).
7. The IRB may request that one or more of the additional elements of consent (as stated in 45 CFR 46.116(b)(1-6)) and 21 CFR 50.25(b)(1-6) also be provided to participants in the following instances:
 - a. The consent form should include a statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or becomes pregnant) which are currently unforeseeable when the research involves procedures that have limited experience in humans and in all research protocols that involve an investigational drug or device.
 - b. The consent form should include the anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent when the protocol describes situations where participants should be withdrawn from the research or if

it is reasonable to expect that participants will be withdrawn from the research without their consent.

- c. The consent form should outline any additional costs to the participant that may result from participation.
 - d. The consent form should state the consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant when withdrawal from the research might place a participant at risk of harm.
 - e. The consent form should include a statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant.
 - f. The consent form should state the approximate number of participants involved in the study when a reasonable person would find the information useful in making a decision to participate in the research.
 - g. In addition, when appropriate, the consent form should reflect Missouri State Law (RSMo Chapters 565.188 (mandatory reporting of elder abuse) and 210.115 (mandatory reporting of child abuse)).
8. Informed consent must be documented by the use of a written consent form approved by the IRB and signed and dated by both the participant or the participant's legally authorized representative and the individual obtaining consent unless the IRB has approved a waiver of signed consent in accordance with Section VII(C) of this Policy. Consent must be documented in one of the following manners:
- a. A written consent document that embodies the elements of informed consent required in 45 CFR 46.116(a)(1-8) and 21 CFR 50.25(a)(1-8). This form may be read to the participant or the participant's legally authorized representative, but in any event, the PI/PD (or designee when consent by a designee has been approved by the IRB) must give either the participant or the representative adequate time to read the consent document before it is signed; or
 - b. A "short form" written consent document stating that the elements of informed consent required by 45 CFR 46.116 and 21 CFR 50.26 have been presented orally to the participant or the participant's legally authorized representative. In addition, the short form requires the following:
 - i. The elements of consent have been presented orally
 - ii. A witness to the oral presentation who is conversant in both English and the language of the participant;
 - iii. An IRB-approved written summary of what is to be said to the participant or the representative This summary must include the basic and any required additional elements of consent
 - iv. The short form must be signed and dated by the participant or their legally authorized representative;
 - v. The witness must sign and date the short form and a copy of the summary;
 - vi. The person obtaining consent must sign and date a copy of the summary; and
 - vii. A copy of the summary and short form must be given to the participant or their legally authorized representative.

9. The IRB may approve a process that allows the consent document to be delivered by mail or facsimile to the potential participants or the potential participant's legally authorized representative. It is acceptable to conduct the consent conversation by telephone provided the potential participant or his/her legally authorized representative can read the consent form as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.
 10. When documented consent is required by the IRB, a signed and dated copy of the consent form must be given to the person signing the form.
 11. Current IRB approval will be documented by a stamp that indicates the dates of IRB approval and expiration of IRB approval.
- B. Waiver or alteration of the requirement to obtain informed consent⁵⁰
1. A waiver or alteration of informed consent will be granted only when a fully convened committee or expedited reviewer finds that the research is not subject to FDA regulations and meets the required conditions stated in 45 CFR 46.116(c) or 45 CFR 46.116(d).
 2. When approving a waiver or alteration of informed consent, the IRB minutes will document the justifications and findings regarding the determinations stated in 45 CFR 46.116(c) or 45 CFR 46.116(d). In the case of research that may be reviewed by expedited procedure, these determinations will be documented on the expedited reviewer sheet.
 3. FDA regulations allow waiver of consent if research meets the criteria specified in 21 CFR 50.23 or 21 CFR 50.24 and HHS regulations allow a waiver of consent if research meets the criteria specified in 45 CFR 46 "Waiver of Informed Consent Requirements in Certain Emergency Research."⁵¹ See Section VIII(G)(8)(c) for a description of the specific requirements for these special circumstances.
- C. Waiver of the requirement for written documentation of consent⁵²
1. For research that is subject to HHS regulation only, a waiver of signed consent will be granted only when the fully convened committee or expedited reviewer finds that the required conditions stated in 45 CFR 46.117(c)(1) or 45 CFR 46.117(c)(2) have been met.
 2. For research that is subject to FDA and HHS regulation, a waiver of signed consent will be approved only when the findings stated in 45 CFR 46.117(c)(1) and 21 CFR 56.109(c)(1) have been met.
 3. When the IRB considers waiving the requirement to obtain written documentation of consent, the IRB will review a written description of the information that will be provided to participants.
 4. When approving a waiver of signed consent the IRB minutes will document the justifications and findings regarding the determinations stated in 45 CFR 46.117(c)(1), 45 CFR 46.117(c)(2), or 21 CFR 56.109(c)(1). In the case of research that may be reviewed by expedited procedure, these determinations will be documented on the expedited reviewer sheet.
 5. In cases in which the documentation requirement for consent is waived, the IRB may require the PI/PD to provide participants with a written statement regarding the research.
- D. Additional considerations for studies involving Protected Health Information (PHI)

1. Studies that involve access to or collection of PHI within the covered entities of WU/BJH/SLCH require consideration of additional items. In these instances, the IRB must find that:
 - a. Appropriate authorization is obtained from research participants or their effective representative for the use or disclosure of their PHI as required in 45 CFR 164.508(a); or
 - b. The IRB has approved a waiver of such authorization in accordance with 45 CFR 164.512(i)(1)(i); or
 - c. The PHI will be contained in a limited dataset with appropriate safeguards to maintain privacy as defined in 45 CFR 164.514(e) and a data use agreement has been executed; or
 - d. The PHI will be deidentified as defined in 45 CFR 164.514(a).
2. In addition to the required and additional elements of consent described in 45 CFR 46 and 21 CFR 50, protocols involving PHI will include the following elements required for HIPAA authorization as stated in 45 CFR 164.508(c):
 - a. A description of the PHI to be collected as part of the research;
 - b. A description of the person or classes of persons authorized to use or disclose the PHI;
 - c. A description of the person or classes of persons who may receive the information and the purpose(s) for each disclosure;
 - d. An expiration date or event of the authorization for use and disclosure (if any);
 - e. A statement of the participant's right to revoke authorization and a contact person for that purpose;
 - f. Notice that disclosure of PHI may result in loss of protection to subsequent disclosure; and
 - g. Limitations, if any, on a participant's access to their records during the study.
3. In instances when research involves use and/or disclosure of PHI, a waiver of authorization will be approved only when the following criteria stated in 45 CFR 164.512(i)(2)(ii) have been met:
 - a. The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals based on:
 - i. The provision of an adequate plan to protect the identifiers from improper use and disclosure.
 - ii. The provision of an adequate plan to destroy the identifiers at the earliest possible opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.
 - iii. The provision of adequate written assurances that the PHI information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project or for other research for which the use or disclosure of PHI would be permitted by law.
 - b. The research could not be practicably conducted without the waiver.
 - c. The research could not be practicably conducted without access to and use of the PHI.

VIII. Special Categories of Research

- A. Research Involving Pregnant Women, Human Fetuses, and Neonates⁵³
1. The IRB will ensure that all non-exempt federally funded research that involves pregnant women, human fetuses, and neonates complies with the additional safeguards and requirements set forth in Subpart B of 45 CFR 46. Non-exempt federally funded research involving pregnant women or human fetuses will be approved only when the conditions outlined in 45 CFR 46.204 (a-j) have been met. Non-exempt federally-funded research involving neonates will be approved only when the applicable conditions outlined in 45 CFR 46.205(a-d) have been met.
 2. Federally funded research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates will be sent to the Secretary of HHS for review. The Secretary will determine the approvability of the research based on the conditions stated in 45 CFR 46.207(b).
 3. Research involving, after delivery, the placenta, the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus, will be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities (see Missouri Statute Chapter 188, Section 188.036).
 4. When reviewing research that involves pregnant women, human fetuses, or neonates, the IRB will ensure that there is adequate expertise and related professional competency among the members of the Committee. If necessary, the IRB may invite nonvoting members selected because of special expertise to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members. In the case of research that may be reviewed by expedited procedure, these determinations will be documented on the expedited reviewer sheet.
 5. When approving research that involves pregnant women, human fetuses, neonates of uncertain viability, the IRB minutes will document the justifications and findings regarding the determinations stated in Subpart B of 45 CFR 46.
 6. Informed consent requirements
 - a. Informed consent for research that involves pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates will be obtained from the mother and father (if necessary) as prescribed in Subpart B.
 - b. According to Missouri State law (Chapter 431, Section 431.061), pregnant minors and/or mothers are considered legally capable of providing consent.
 7. In regards to research in which pregnancy is coincidental to participant selection and the research includes women of childbearing potential, when appropriate, the participants should be informed of the currently unforeseeable risks to the participant, fetus, or nursing infant. In addition, the IRB will determine whether:
 - a. the participant should be advised to avoid pregnancy or nursing during or following participation in the research and/or notify the PI/PD immediately should the participant become pregnant; or

- b. The PI/PD should specifically exclude pregnant women from the research and/or require specified methods of contraception during and/or following participation in the research.
- B. Research Involving Prisoners⁵⁴
 1. Because prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision to participate in research, the IRB will ensure that all research that involves prisoners complies with the additional safeguards and requirements set forth in Subpart C of 45 CFR 46. Research involving prisoners will only be approved when the conditions outlined in 45 CFR 46.305 and 45 CFR 46.306 have been met.
 2. In the review of research involving prisoners, the IRB will consider the prisoner-specific definition of minimal risk as stated in 45 CFR 46.303(d).
 3. When reviewing research that involves prisoners, including new submissions, continuing reviews, modifications and unanticipated problems, the IRB will meet the following specific requirements in addition to satisfying the requirements for IRB membership outlined in 45 CFR 46.107:
 - a. A majority of the committee members will have no association with the prison involved; and
 - b. At least one member of the reviewing committee will be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity. The prisoner representative will be included on the list of registered IRB members filed with OHRP.
 4. The IRB will employ the use of the expedited review mechanism only for minor modifications to ongoing research involving prisoners and continuing review of research involving prisoners that meets expedited categories 8(a), (b) or (c) as defined in HHS guidance, "Categories of Research That May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure" (63 FR 60364-67 11/9/98). The prisoner representative will contribute to the expedited review to confirm that the request meets the criteria for expedited review and that the research continues to meet the regulatory criteria for inclusion of prisoners.
 5. When approving research that involves prisoners, the IRB minutes will document the justifications and findings regarding the determinations stated in Subpart C of 45 CFR 46. In the case of research involving prisoners that qualifies for review by expedited procedure, as indicated in this policy, these determinations will be documented on the expedited reviewer sheet.
 6. When a participant becomes a prisoner while participating in a research protocol, the PI/PD is responsible for immediately reporting the situation to the the IRB. All research activities with that participant should cease unless it is the best interest of the participant to remain in the research study while incarcerated. If the PI/PD wishes to have the prisoner continue to participate in the research, the IRB will arrange re-review of the protocol by a Committee that includes a prisoner representative. At the time of re-review, the Committee will either:
 - a. Approve the involvement of the prisoner-participant in accordance with the requirements and conditions in Subpart C of 45 CFR 46; or
 - b. Require that the prisoner-participant be withdrawn from the research.
 7. Only federally funded research involving prisoners will be sent to OHRP for certification.

- C. Research Involving Children (as defined in Subpart D)⁵⁵
1. In determining applicability of Subpart D, the IRB will take into consideration the legal age for consent to treatments or procedures involved in the proposed research, under the applicable law of the jurisdiction in which the research will be conducted. In instances where research will take place in jurisdictions outside of Missouri (including other states and other nations), the IRB will consult with WU legal counsel to determine the legal age for the proposed treatments/procedures within the specific jurisdiction.
 2. In determining who other than a parent may consent on behalf of a child to their participation in research, the IRB will take into consideration who under the applicable law of the jurisdiction in which the research will be conducted meets the DHHS and FDA definition of a “guardian”, that is who under the applicable law of the jurisdiction in which the research will be conducted is authorized to consent to general medical care on behalf of the child. In instances where research will take place in jurisdictions outside of Missouri (including other states and other nations), the IRB will consult with WU legal counsel to determine who is authorized to consent to general medical care on behalf of the child within the specific jurisdiction.
 3. All research involving children will comply with the additional safeguards and requirements set forth in Subpart D of 45 CFR 46 and Subpart D of 21 CFR 50 (see HRPO Form E). Research involving children will only be approved by the IRB when the applicable conditions outlined in 45 CFR 46.404 – 406 and 21 CFR 50.51-53 have been met.
 4. Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children will be sent to the Secretary of HHS for review. The Secretary will determine the approvability of the research based on the conditions stated in 45 CFR 46.407 (a-b) and 21 CFR 50.54(a-b).
 5. When reviewing research that involves children, there will be adequate expertise and related professional competency among the members of the Committee. If necessary, the IRB may invite nonvoting members selected for their special expertise to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.
 6. When approving research that involves children, the IRB minutes will document the justifications and findings regarding the determinations stated in Subpart D of 45 CFR 46 and Subpart D of 21 CFR 50. In the case of research that may be reviewed by expedited procedure, these determinations will be documented on the expedited reviewer sheet.
 7. Requirements for assent from children
 - a. In accordance with 45 CFR 46.408(a) and 21 CFR 50.55(a), the IRB must determine that adequate provisions have been made for soliciting the assent of children when in the judgment of the IRB the children are capable of providing assent. Assent is required for all children who can understand spoken language unless the IRB determines that one of the conditions below applies and grants a waiver of assent. Research protocols targeting children should include a description of the procedure used to obtain assent.
 - b. The IRB may determine that assent is not a necessary condition for proceeding with the research if:

- i. The capability of some or all of the children is so limited that they cannot reasonably be consulted. (When determining capacity to consent, the IRB will take into account the age, maturity, and psychological state of the child. This judgment may be made for all children involved in the research or for each child, as the IRB deems appropriate); or
 - ii. That the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well being of the children and is available only in the context of the research; or
 - iii. The research meets the required criteria for waiver of consent stated in 45 CFR 46.116(d)(1-4) and 21 CFR 50.55(d).
 - c. When the IRB determines that the participant population will be capable of providing assent, an oral or written assent process may be approved depending on the appropriateness for the study and the study population. When a study has an approved assent process and it is inappropriate to assent a specific child, the PI/PD (or designee when consent by a designee has been approved by the IRB) must document why assent is not appropriate.
- 8. Requirements for permission of each child's parent(s) or legally authorized representative
 - a. In accordance with 45 CFR 46.408(b) and 21 CFR 50.55 (e), the IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent(s) or guardian.
 - b. Parents or guardians must be provided with the basic elements of consent as stated in 45 CFR 46.116(a)(1-8) and 21 CFR 50.25(a)(1-8) and any additional elements the HRPO deems necessary.
 - c. The IRB may find that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404 (21 CFR 50.51) or 45 CFR 46.405 (21 CFR 50.52). The IRB's determination of whether consent must be obtained from one or both parents will be documented in the meeting minutes or, in the case of expedited research, on the reviewer sheet.
 - d. Consent from both parents is required for research to be conducted under 45 CFR 46.406 (21 CFR 50.53) and 45 CFR 46.407 (21 CFR 50.54) unless:
 - i. One parent is deceased, unknown, incompetent, or not reasonably available; or
 - ii. When only one parent has legal responsibility for the care and custody of the child.
 - e. The IRB may waive the requirement for obtaining consent from a parent or legal guardian if:
 - i. The research meets the provisions for waiver in 45 CFR 46.116(d)(1-4) or
 - ii. In accordance with 45 CFR 46.408(c): The IRB determines that the research protocol is designed for conditions or a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), provided an appropriate mechanism for protecting the children who will participate as participants in the research is substituted, and that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend

- upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.
- f. Permission from parents or legal guardians must be documented in accordance with and to the extent required by 45 CFR 46.117 and 21 CFR 50.27.
9. Research involving children who are wards of the state or any other agency, institution, or entity
 - a. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 (21 CFR 50.23) and 45 CFR 46.407 (21 CFR 50.54) only if:
 - i. The research is related to their status as wards; or
 - ii. conducted in school, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.
 - iii. An advocate has been appointed for each child who is a ward in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*.
 - The advocate is an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research.
 - The advocate is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian.
 - b. Any research that targets or includes individuals who are Wards of the State must abide by provisions set forth by the appropriate authorities of the State in which research procedures take place.
- D. Research involving adults who are cognitively impaired or decisionally-impaired
 1. Cognitively-impaired or decisionally-impaired adults are individuals who have a diminished capacity for judgment and reasoning. Other individuals may be considered cognitively-impaired or decisionally-impaired or have limited decision-making ability because they are under the influence of drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have disabling physical handicaps.
 2. In addition to considerations associated with the criteria for approval, the IRB will take into consideration the following additional points when reviewing research involving adults with impaired cognitive or decision-making capacity:
 - a. Whether the research could be conducted without these individuals.
 - b. How the protocol addresses the needs of this vulnerable population
 - c. Adequacy of the proposed initial and ongoing consent and assent processes.
 - d. Who under state or local law meets the DHHS and FDA definition of "legally authorized representative" under the applicable law of the jurisdiction in which the research will be conducted. In instances where research will take place in jurisdictions outside of Missouri (including other states and other nations), the IRB will consult with WU legal counsel to determine the requirements within the specific jurisdiction.
- E. WU Undergraduate Students as research participants

1. Psychology Department. Investigators in the Department of Psychology who wish to recruit students as participants in their studies must follow the requirements of the Psychology Department Subject Pool Policy. PIs/PDs from other Schools/Departments may utilize the undergraduate participant pool upon permission of the Department of Psychology Human Subjects Pool Coordinator.
 2. Olin School of Business. Investigators in the Olin School of Business who wish to recruit students as participants in their studies must follow the requirements of the Olin School Subject Pool Policy.
 3. The IRB has reviewed and approved each of the above-mentioned Policies to ensure students' voluntary participation through recruitment processes which are neither coercive nor suggest undue influence.
- F. Economically or Educationally Disadvantaged
1. The IRB will review research targeted at groups of individuals who are economically or educationally disadvantaged to assure that participation is voluntary, free of coercion, duress, or undue inducement.
 2. In reviewing research in which economically or educationally disadvantaged individuals are likely to be recruited, the IRB will specifically consider the following:
 - a. Recruitment and consent processes provide sufficient detail for members to assess the voluntary participation of participants.
 - b. All study documents, including materials read to participants or provided in writing, are appropriate to the population and will be easily understood.
 - c. Any reimbursement for participation is reasonable in relation to the time required.
- G. Research involving an Investigational Drug or Device
1. Research involving use of an investigational drug requires an Investigational New Drug (IND) from the Food and Drug Administration (FDA) unless the study is exempt from the requirements for an IND by meeting all of the conditions stated in 21 CFR 312.2(b)(1).
 2. Research involving the evaluation of the safety or effectiveness of a device requires an Investigational Device Exemption (IDE) from the FDA, unless:
 - a. The study is exempt from the requirements for an IDE by meeting all of the conditions stated in one of the seven categories in 21 CFR 812.2(c); or
 - b. The device under study is determined to be a non-significant risk device and the abbreviated IDE requirements as defined in 21 CFR 812.2(b) are met.
 3. The Executive Chair (or designee) will determine if a protocol involving an investigational drug meets the exemption criteria as defined in 21 CFR 312.2(b)(1). If the exemption criteria are not met, the Executive Chair (or designee) will inform the PI/PD, in writing, that a formal IND determination by the FDA is required and provide a rationale for this decision. The PI/PD will be required to contact the FDA to either obtain an IND or written documentation that an IND is not necessary before any further review by the IRB will occur.
 4. The Executive Chair (or designee) will determine if a protocol involving an investigational device meets the exemption criteria as defined in 21 CFR 812(c). If the exemption criteria are not met one of the following will occur:

- a. The protocol will be scheduled for review by a fully convened committee to determine if the device is a non-significant risk device as outlined under the abbreviated IDE requirements in 21 CFR 812(b); or
 - b. The PI/PD will be informed by the Executive Chair (or designee), in writing, that a formal IDE determination by the FDA is required and provide a rationale for this decision. The PI/PD will be required to contact the FDA to either obtain an IDE or written documentation that an IDE is not necessary before any further review by the IRB will occur.
- 5. Protocols involving an investigational device that may be considered a non-significant risk device as outlined under the abbreviated IDE requirements in 21 CFR 812 (b) will be reviewed by a fully convened committee. The committee will determine if the proposed use of the investigational device does or does not meet the regulatory definition of a significant risk device. This determination will be made in addition to the research risk determination of “greater than minimal” or “minimal risk”. The significant risk/nonsignificant risk determination and the rationale for the IRB’s decision will be noted in the meeting minutes. If the IRB determines that the research involves an investigational device that is a significant risk device, the PI/PD will be notified in writing that a formal IDE determination by the FDA is required. IRB approval will be held contingent pending receipt of the FDA determination.⁵⁶
- 6. Additional requirements for research involving an investigational drug or device: All protocols involving an Investigational Drug (IND) or Investigational Device (IDE) require consideration and satisfaction of the pertinent FDA regulations, as applicable (21 CFR 50, 21 CFR 56, 21 CFR 312, and 21 CFR 812, and 45 CFR 46). Storage, dispensing, and control of investigational drugs or devices will be in accordance with the WU policy titled, “Investigational Drug/Device Accountability”. Instances when investigators propose alternate plans for storage, dispensing, and control of investigational agents will be reviewed and approved by the IRB on a case-by-case basis as part of the protocol review process. When the WU PI/PD holds the IND or IDE, the following additional requirements apply:
 - a. The PI/PD must submit documentation that the proposed preparation has been reviewed and is compliant with Current Good Manufacturing Practices (Applicable regulations for drugs: 21 CFR 210 & 211; for devices: 21 CFR 820).
 - b. The PI/PD must attend a mandatory educational session that reviews all sponsor responsibilities as stated in:
 - i. Drugs or devices: 21 CFR §11 (Electronic records and electronic signature) and 21 CFR §54 (Financial Disclosure by Clinical Investigators).
 - ii. Drugs and Biologics: 21 CFR §210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General), 21 CFR §211 (Current Good Manufacturing Practice for Finished Pharmaceuticals), 21 CFR §312 (Investigational New Drug Application), 21 CFR §314 (Drugs for Human Use), 21 CFR §320 (Bioavailability and Bioequivalence Requirements), 21 CFR §330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded), 21 CFR §601 (Biologics Licensing).

- iii. Devices: 21 CFR §807 (Establishment Registration and Device Listing for Manufacturers and Initial Importers Of Devices), 21 CFR §812 (Investigational Device Exemptions), 21 CFR §814 (Premarket Approval of Medical Devices), 21 CFR §820 (Quality System Regulation), 21 CFR §860 (Medical Device Classification Procedures).
- 7. Protocols involving an investigational drug or device will undergo initial and continuing review at a convened meeting unless the protocol meets the criteria for review by expedited procedure.
- 8. Consent for FDA-regulated research will be obtained as stated in Section VII (A) of this Policy. The consent form will identify the test article as investigational and will inform participants that the FDA may inspect research records.
- 9. Emergency treatment with an investigational drug or device⁵⁷
 - a. In accordance with FDA regulations, the IRB may allow for the emergency use of an investigational drug or device if the situation meets the definition of “Emergency Use” as stated in 21 CFR 56.102(d) and if the emergency use is reported to the IRB within five working days of the actual use of the drug or device.
 - b. In general, the IRB prefers to be notified prior to an emergency use of an investigational drug or device. If time permits, the request should be submitted to the IRB. If deemed to meet the regulatory and any applicable institutional requirements, the Executive Chair or designee will acknowledge the request. A follow up report should be submitted to the IRB within 5 working days of the actual use of the drug or device.
 - c. If time does not permit for prior notification to the IRB of the emergency use of an investigational drug or device, notification to the IRB is required within 5 working days of the emergency use.
 - d. A waiver of consent for emergency use of an investigational drug or device will be approved only when the research meets the criteria specified in 21 CFR 50.23 and HHS, “Waiver of Informed Consent Requirements in Certain Emergency Research.”⁵⁸
 - e. When emergency medical care is initiated without IRB approval, data regarding such care may be reported the Sponsor and the FDA but may not be included in any report of a prospectively conceived research activity.
 - f. Subsequent use of the test article must be reviewed by the IRB. However, the FDA and the IRB acknowledge that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene to review the situation. In instances when the IRB has received more than one request for emergency treatment (multiple requests from the same researcher or isolated requests from more than one researcher), the IRB will review the request but will ask the researcher to submit a protocol for review by a fully convened committee for subsequent treatments. In instances where a second researcher requests approval for an identical use, the IRB will suggest that he/she collaborate with the PI/PD who made the initial request.
- 10. Compassionate Use of an Investigational Device for a Serious Disease or Condition
 - a. There are circumstances in which an investigational device is the only

option available for a patient faced with a serious, albeit not life-threatening, disease or condition. In these circumstances, the FDA uses regulatory discretion in determining whether such use of an investigational device should occur.

- b. A request for compassionate use of an investigational device for a serious disease or condition should be submitted to the IRB and the FDA.
 - c. Concurrence from the Executive Chair or designee is required prior to submitting for FDA approval.
 - d. FDA approval must be obtained prior to the use of the investigational device.
 - e. The PI should develop an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient.
 - f. If any problems occur as a result of the device use they should be reported to the IRB as soon as possible.
11. Prospective Research in Emergency Settings – FDA-Regulated Research: The IRB may approve a protocol involving an investigational drug or device without requiring that informed consent of all participants be obtained only when the IRB and a licensed physician find and document that the following criteria below have been met. The licensed physician must be a member of or consultant to the IRB and may not otherwise be participating in the clinical investigation.
- a. The human participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
 - b. Obtaining informed consent is not feasible because:
 - i. The participants will not be able to give their informed consent as a result of their medical condition;
 - ii. The intervention under investigation must be administered before consent from the participants' legally authorized representatives is feasible; and
 - iii. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
 - iv. Participation in the research holds out the prospect of direct benefit to the participants because:
 - A. Participants are facing a life-threatening situation that necessitates intervention
 - B. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual participants; and
 - C. Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
 - c. The clinical investigation could not practicably be carried out without the waiver.

- d. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
- e. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to an individual's participation in the clinical investigation.
- f. Additional protections of the rights and welfare of the participants will be provided, including, at least:
 - i. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn;
 - ii. Public disclosure to the communities in which the clinical investigation will be conducted and from which the participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
 - iii. Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
 - iv. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
 - v. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant's family member who is not a legally authorized representative, and asking whether he or she objects to the participant's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
 - vi. The IRB will ensure that procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.
 - vii. The IRB will ensure that there is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not

reasonably available, a family member, that he or she may discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the participant's condition improves, the participant is also to be informed as soon as feasible. If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant's legally authorized representative or family member, if feasible.

- g. If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.
12. Prospective Research in Emergency Settings – research not regulated by the FDA:⁵⁹ The IRB may approve a waiver of consent for prospective research in emergency settings that is not FDA-regulated only when both the research and the waiver of informed consent have been approved by the full board, the committee has determined and documented that the research *is not subject* to regulations codified by the FDA at 21 CFR Part 50, and the committee has found, documented, and reported to OHRP that the following conditions have been met relative to the research:
- a. The human participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions;
 - b. Obtaining informed consent is not feasible because:
 - i. the participants will not be able to give their informed consent as a result of their medical condition;
 - ii. the intervention involved in the research must be administered before consent from the participants' legally authorized representatives is feasible; and
 - iii. there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
 - c. Participation in the research holds out the prospect of direct benefit to the participants because:
 - i. participants are facing a life-threatening situation that necessitates intervention;
 - ii. appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual participants; and
 - iii. risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

- d. The research could not practicably be carried out without the waiver;
- e. The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review;
- f. The committee has reviewed and approved informed consent procedures and an informed consent document in accord with Sections 46.116 and 46.117 of 45 CFR Part 46. These procedures and the informed consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to an individual's participation in the research consistent with OPRR Report Number 97-01 Informed Consent Requirements in Emergency Research (b)(7)(v);
- g. Additional protections of the rights and welfare of the participants will be provided, including, at least:
 - i. consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the participants will be drawn;
 - ii. public disclosure to the communities in which the research will be conducted and from which the participants will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;
 - iii. public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;
 - iv. establishment of an independent data monitoring committee to exercise oversight of the research; and
 - v. if obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant's family member who is not a legally authorized representative, and asking whether he or she objects to the individual's participation in the research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
- h. In addition, the committee is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the participant, or if the participant remains

incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she may discontinue the individual's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a legally authorized representative or family member is told about the research and the participant's condition improves, the participant is also to be informed as soon as feasible. If a participant is entered into research with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the participant's legally authorized representative or family member, if feasible. (For the purposes of this waiver "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.)

13. Humanitarian Use Device (HUD)⁶⁰

- a. Treatment with a HUD will be initially reviewed by a fully convened committee. At the time of review, the IRB will determine if written consent from participants for use of the HUD is necessary (see HRPO Guidelines for Humanitarian Device Exemptions). If determined by the committee at the time of initial review continuing review may be conducted by expedited procedure.
- b. If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior IRB approval. In this instance, the PI/PD is required to provide written notification of the use to the Executive Chair within five days after use of the device. The IRB requires that written notification include identification (specification without identifiers) of the patient, the date on which the device was used, and the reason for the use.
- c. It is the responsibility of the PI/PD to notify the FDA if the IRB were ever to withdraw approval for use of a HUD. The FDA should be notified within five days of notification of the withdrawal of approval.
- d. PI/PD's are reminded that HDEs are for clinical use only and HUDs can be used only for purposes outlined in IRB application.

IX. WU Principal Investigators/Project Directors (PI/PDs)

- A. Qualifications
1. All personnel performing any procedures associated with a research protocol must have appropriate training and expertise.
 2. Individuals performing specific functions or procedures should have the necessary licensure and/or credentials to conduct the activity in accordance with the research protocol. Exceptions to this policy would require IRB approval and approval from the appropriate WU institutional authority.
 3. Medications administered as part of this research should be administered in accordance with the applicable licensure requirements as found in RSMo. Chapter 324 et seq.
 4. The PI/PD's qualification to conduct research is documented by virtue of his/her faculty, staff, or student status and approval of the Dean/Department Chair or designee provided at the time of a new application.
 5. The PI/PD must have adequate resources including funding, facilities, staff, and equipment to conduct proposed research.
 6. If research is conducted by a WU undergraduate or graduate student the IRB requires that the research be sponsored by a member of the WU full-time faculty and approved by the WU Sponsor's Dean/Department Chair or designee.
- B. Education Requirements
1. The IRB requires that PI/PDs and research personnel comply with the WU policy regarding education related to the protection of the rights and welfare of research participants and HIPAA compliance (when applicable) prior to conducting research. Completion of the required CITI modules constitutes adequate training (located at <https://aisinfo.wustl.edu/ra.html>).
 2. It is the responsibility of the PI/PD to ensure that research personnel are qualified and adequately trained in the protection of the rights and welfare of human participants.
 3. The HRPO provides ongoing educational opportunities to PI/PDs and research personnel. Examples of education provided include presentations provided in various venues including but not limited to, the bimonthly Question and Answer sessions, the yearly Ethics Series, individual or group educational sessions provided by request, informational broadcasts via Research News and through guidelines and other information available on the HRPO website (<http://hrpohome.wustl.edu>).
 4. WU faculty who serve as research sponsors or advisors are expected to understand the regulatory and ethical considerations for research with human participants, and as such, must comply with these educational requirements whether or not they are engaged in the research.
- C. Finder's Fees
1. PI/PDs and research personnel may not individually receive incentive payments or finder's fees on a per participant basis. PI/PDs may not accept payments that are prospective incentives based solely on participant recruitment.
 2. Finder's fees may not be paid to any individual referring or recruiting prospective participants. Finder's fees include any payment or gift to an individual who identifies a prospective subject.

3. PI/PDs may accept monetary rewards that are offered by the sponsor only after the research is closed to enrollment and only if the reward is directed to the research team as a whole and under the control of the Dean or Department Chair (e.g. funds allocated for purchasing educational materials or to support attendance at educational conferences).

D. Financial Conflicts of Interest

1. WU requires that all employees comply with the WU Conflict of Interest Policies.
2. The IRB requires all individuals (which includes respective spouse and dependent children) engaged in the research to disclose any financial interests that the individual, or the individual's spouse or dependent children, have with the sponsor of the study, the supporting organization, or company that owns or licenses the technology being studied.
3. When a financial interest exists, the financial interest will need to be reviewed, approved, and, if necessary, managed by the Conflict of Interest Review Committee (CIRC). A summary of the CIRC findings and recommended management strategy will be provided to the IRB members for review and discussion at a full board meeting or will be reviewed by an expedited reviewer if the research qualifies for review by expedited procedure. As part of the review, the IRB has the authority to request additional actions to manage the conflict of interest to increase protections for the research participants. If additional actions are requested this information will be communicated to the CIRC. The IRB has the final authority to determine whether the research with the financial interest and the management plan, if any, allow the research to be approved.
4. Documentation of the CIRC review and the IRB review of the financial conflict of interest is required in order for the IRB to approve the research.
5. The IRB may require disclosure of the financial interest to participants in the consent form if a financial conflict of interest, as defined by the WU Conflict of Interest Policy and the Conflict of Interest in Clinical Research Policy is identified.

E. IRB Approval

1. The IRB approval will be obtained before implementation of any research involving human participants, including review of identifiable data, records, tissues, or other derived materials.
2. Approval also will be obtained before initiating any change to previously-approved research except when necessary to eliminate apparent, immediate hazards to participants.
3. Changes initiated without IRB approval to alleviate an immediate hazard should be submitted to the IRB immediately after the occurrence. The event is reviewed by the IRB to determine whether the change was consistent with ensuring the participants' continued welfare. These events may require review by a fully convened committee if the change is considered to be more than minor.
- 4.

F. Change in the PI/PD

1. Changes in PI/PD are treated as modifications to previously approved research and must be approved by the IRB before implementation of the change.
 2. Requests to change the PI/PD must be approved by the IRB after prior approval is obtained from the original PI/PD and the authorized Dean, Department Chair, or designee.
 3. Student-conducted research requires additional prior approval of the Faculty Sponsor.
 4. In studies where active participation is ongoing, participants should be notified about the change in PI/PD, as this is a change in the original agreement (informed consent) between the parties. Participants may be notified by letter, phone call, or other mode of communication, approved by the IRB.
- G. Commercial Products from Human Tissue: When the intent of the research is to develop a commercial product, such information will be disclosed in the informed consent document.
- H. Responsible Conduct of Research
1. All members of the WU community who are engaged in research with human participants are expected to comply with the highest standards of ethical and professional conduct in accordance with Federal and state regulations and WU Institutional and IRB policies.
 2. Failure on the part of the PI/PD, or any member of the study team to comply with these policies will result in IRB and/or WU intervention appropriate to the infraction, in accordance with IRB Policies and Procedures.
- I. IRB review of grant applications
1. For sponsored research, the IRB will ensure that the research scope described in the grant application or proposal is consistent with any corresponding protocol(s).
 2. "Scope" includes change in direction, type of research or training, or other areas that constitute a significant change from the aims, objectives, or purposes of the approved research.
- J. HIPPA Minimum Necessary Standard
1. The research team will only collect information essential to the study and in accordance with this University Policy.
 2. To the greatest extent possible, access to the information will be limited within the research team.
 3. If protected health information is used or created, it will not be re-used or disclosed to any other person or entity, except as required by law, research oversight, or those uses outlined in the application.
- K. Informed Consent: The rights and welfare of human participants and the methods for obtaining their voluntary consent to participate in research should be carried out in accordance with Federal regulations and Washington University Institutional and IRB policies, including Washington University's Federalwide Assurance with the Department of Health and Human Services Office for Human

Research Protections (OHRP). This includes the information listed below, along with the information in Section VII.:

1. Information provided during the consent process should be discussed with prospective participants to ensure that they understand the nature of the research and can voluntarily decide to participate, without risk of coercion or undue influence.
2. If any language barriers or other impediments to communication exist, appropriate measures should be taken to ensure the participant's understanding. When consenting non-English speaking participants, consent should occur in the native language in the format approved for the study.
3. Discussions regarding the research and each participant's desire to continue to participate should continue throughout their participation in the study.
4. When children participate in research, their assent should be obtained in accordance with the provisions approved by IRB.
5. When written documentation of consent is required, the consent form should be signed and dated by both the research participant and the individual who obtained the consent. A signed copy should be provided to the participant.
6. The individual obtaining consent must be a member of the study team and appropriately trained and qualified.
7. Any information provided to participants in the form of consent and written assent documents, scripts, and debriefing forms (as may be required by HRPO) should bear the HRPO stamp of approval.
8. Contact information for the PI/PD and the HRPO should be provided to research participants such that participants are aware of whom to contact for information and or complaints should the need arise. This information should be clearly stated in the consent form, or when the IRB waives written documentation of consent, provided orally or in a written information sheet, as may be required by the IRB. The PI/PD is responsible for promptly responding to requests for information from participants as well as follow up regarding participant complaints.

L. Rights of Research Participants

1. Only bona fide members of the study team that are listed on the IRB application are ordinarily authorized to be present during research procedures.
2. The only exceptions to this rule are when: (i) a participant specifically requests the presence of his/her advocate and the research permits the advocate's presence; (ii) research involves standard clinical procedures in which case it is appropriate for standard procedures to be carried out by qualified, non-research staff according to customary standards of care; or (iii) the participant gives permission for the research to be observed by students, trainees, and/or faculty and the experience is consistent with the educational mission of Washington University. Permission of the participant may be obtained orally.
3. Study team members would not include: the sponsor, other research sites, outside labs, independent statistician, colleagues (clinical associates).

- M. Referrals: If during the course of the research study, it becomes apparent that the participant needs to be referred for further services, the PI/PD should make such referral(s).
- N. Continuing Review
1. Federal regulations require that research involving human participants be reviewed by the IRB at least annually.
 2. As a courtesy to investigators, the HRPO issues renewal notices before the study is due to expire. To allow adequate time for review, it is very important to submit your continuing renewal paperwork 6 weeks prior to the date of IRB approval expiration.
 3. If IRB approval expires all research activities must stop and new participants may not be enrolled. Any continuation of treatment or follow-up after IRB approval has expired requires IRB approval. Requests to continue treatment or follow-up should be directed to the Executive Chair.
 4. A study may be closed if HRPO has not received a continuing review application or a final report and 30 days have passed since the expiration date of IRB approval. Once HRPO closes a study it will not be re-opened.
- O. Verification of information related to ongoing research
1. The IRB has the right to determine which protocols need verification of specific aspects of the research by sources other than the PI/PD to ensure that no material changes have occurred since the previous IRB review. This verification may occur by:
 - a. Conducting audits or inquiries to collect information, and/or
 - b. Having the IRB or its designee observe the consent process and/or conduct of research.
 2. The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:⁶¹
 - a. Protocols selected at random by HRPO for quality assurance auditing functions
 - b. Complex protocols involving unusual levels or types of risks to participants;
 - c. Protocols conducted by PI/PDs who previously have failed to comply with HHS regulations or the requirements and determinations of the IRB;
 - d. Protocols where concern about the conduct of the study and protection of research participants has been raised based on information provided in continuing review reports or from other sources.
 3. When the IRB or HRPO staff identify a need for verification of information related to ongoing research, the IRB or HRPO staff may request that the Human Subject Research Quality Assurance/Quality Improvement Office conduct such activities (e.g. audits, observations of the consent process) and report findings to the IRB. The assistance of the Human Subject Research Quality Assurance/Quality Improvement Office would not be requested in the case of the HRPO random, not-for-cause audits which are conducted for quality assurance purposes.
- P. Appeal Process
1. Full Board Reviews: The PI/PD has the right to contact the Executive Chair or HRPO staff to request re-review of his/her protocol, reconsideration of

stated contingencies, or reevaluation of points relevant to the regulatory criteria for approval. In these instances, subsequent reviews would be conducted by the original reviewing committee.

2. Expedited Reviews: If a PI/PD does not agree to contingencies recommended by the expedited reviewer, the protocol is referred to the full board.

Q. Record Retention

1. All research records, including signed consent forms, must be kept in their original form at least seven years beyond completion of the study.
2. Additional retention may be required under State and Federal laws or at the request of the study sponsor.
3. Protected Health Information must be stored with at least two safeguards (e.g. a locked cabinet in a locked office) in accordance with the WU HIPAA Policies and WU Security Measures Required to Comply with Privacy Policies.

R. Final Report

1. The PI/PD is required to submit a final report at the conclusion or discontinuation of all IRB approved projects.
2. Protocols may be closed and a Final Report submitted when the following conditions apply:
 - a. All interventions and interactions with the research participant have been completed and
 - i. the data have been stripped of all identifiers (including codes) with which individual identities of participants could be ascertained; or
 - ii. the data remain identifiable but will no longer be used for the current research protocol.
 - b. After a protocol has been closed a new study application must be submitted and approved by the IRB before any identifiable or coded data may be used, even by the same investigator/study team.
3. A protocol may be closed by the HRPO without a final report as described in Section IX (N). Repeated failure to not submit final reports may be considered noncompliance with the WU IRB policies.

S. Ownership of Research Property

1. Washington University owns all intellectual property, including lab notebooks, cell lines and other tangible research property. This includes original research documents, lab notebooks (in any format), interview tapes and transcripts, electronic databases, and all other data and specimens.
2. When a PI/PD leaves WU, all such research property will stay at WU in the custody of a collaborator or the appropriate Dean or Department Head unless prior arrangements have been made and the appropriate institutional approvals have been obtained. (<http://www.wustl.edu/policies/intelprop.html>).

X. Investigator Reporting Requirements and IRB Review of Reportable Events

A. Definitions

1. Unanticipated problem involving risks to participants or others:
 - a. Are unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; and
 - b. Are related or possibly related to participation in the research; and
 - c. Suggest that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
2. Unexpected adverse drug event: Any adverse drug experience (associated with the use of the drug), the frequency, specificity, or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information provided to the participants and the IRB.
3. Unexpected adverse device effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
4. Non-compliance: Failure to follow any applicable regulation or institutional policies that govern human subjects research or failure to follow the determinations of the IRB. Noncompliance may occur due to lack of knowledge or due to deliberate choice to ignore regulations, institutional policies, or determinations of the IRB.
5. Serious non-compliance: Noncompliance that materially increases risks, that results in substantial harm to subjects or others, or that materially compromises the rights or welfare of participants.
6. Continuing non-compliance: A pattern of repeated non-compliance including non-compliant acts, omissions or behavior, that if continued will likely, in the Committee's judgment, materially adversely affect (a) the rights, welfare or safety of research participants, (b) the integrity or validity of the pertinent study(s), or (c) the mission or operation of the HRPO. The pattern may comprise repetition of the same non-compliant action(s), or different non-compliant events. Such non-compliance may be unintentional (e.g. due to lack of understanding, knowledge, or commitment), or intentional (e.g. due to deliberate choice to ignore or compromise the requirements of any applicable regulation, institutional policy, or determination of the IRB).
Report of non-compliance: An instance of non-compliance that does not require further information to confirm.
7. Allegation of non-compliance: An assertion made by a second party that must be proven or supported with evidence to either confirm or deny.

B. Investigator Reporting Requirements

1. The PI/PD is required to notify the IRB promptly of the following events:

- a. Any unanticipated problems involving risks to participants or others which occur at WU, any BJH or SLCH institution or that impacts participants or conduct of the study. This includes:
 - i. Unexpected adverse drug events
 - ii. Unexpected adverse device effects
 - iii. Other unanticipated problems
 (For more information about events that may represent an unanticipated problem see the Office of Human Research Protection's [Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events](#) or the Food and Drug Administration's [Guidance on Adverse Event Reporting to IRBs-Improving Human Subject Protection](#))
 - b. Noncompliance with federal regulations or the requirements or determinations of the IRB
 - c. Receipt of new information that may impact the willingness of participants to participate or continue participation in the research study
2. Timeframe for reporting:
- a. The events described in Section X(B)(1) should be reported within 10 working days of the occurrence of the event or notification to the PI/PD of the event.
 - b. The death of a research participant enrolled at WU/BJH/SLCH that qualifies as a reportable event under X(B)(1) should be reported within 1 working day of the occurrence of the event or notification to the PI/PD of the event.
3. Additional reporting requirements: Audits/Inspections/Inquiry
- a. The PI/PD should immediately contact the HRPO upon notice of any for-cause audit. This notification should occur via email to the Manager of the Education and Compliance Team.
 - b. Follow up information should be provided and include any reports or determinations as a result of the audit.
 - c. For audits by the Food and Drug Administration (FDA), the PI/PD should notify the HRPO within one working day of notice of the audit. This applies to both routine and for-cause audits. After the audit the PI/PD should provide follow up information to HRPO within one working day describing the outcome of the audit, even if there are no findings. If there are findings from the audit supporting documentation should be included, such as a 483 report, warning letter or any other correspondence from the FDA.
 - d. Routine audits/inspections/inquiries that result in findings of noncompliance as defined in this policy should be reported in accordance with Section X(B)(1).
- C. Procedures for Review of Reports of Unanticipated Problems
- 1. The Executive Chair (or designee) will review reports of submitted events to verify that the event represents an unanticipated problem involving risks to participants or others
 - 2. If the report is verified by the Executive Chair (or designee) to constitute an unanticipated problem involving risks to participants or others and the event represents no more than a minimal risk of harm the event is acknowledged by the Executive Chair (or designee) along with requiring any additional actions as described in Section X(C)(5).
 - 3. If the report is verified by the Executive Chair (or designee) to constitute an unanticipated problem involving risks to participants or others and the event

represents more than a minimal risk of harm the event will be reviewed by a fully convened committee.

4. If the event requires full board review, see Section V(B)(10). The convened committee will review the report and determine if i.) the event represents an unanticipated problem involving risks to participants or others and ii) determine if any additional actions are required as described in Section X(C)(5). If the determination made by the convened committee differs from that made by the Executive Chair (or designee), the determination of the convened committee supersedes that made by the Executive Chair (or designee).
5. The Executive Chair (or designee) or convened committee may take the following actions to protect the rights and welfare of participants. These actions may included, but are not limited to:
 - a. No action necessary
 - b. Modification of the study
 - c. Modification of the consent process
 - d. Modification of the consent document
 - e. Providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
 - f. Providing additional information to past participants
 - g. Requiring current participants to re-consent to participation
 - h. Alteration of the frequency of continuing review
 - i. Requiring additional training of the PI/PD
 - j. Referral to the Human Subject Research Quality Assurance/Quality Improvement Office for monitoring of the research or consent process
 - k. Referral to the Research Integrity Officer
 - l. Referral to other institutional entities/offices
 - m. Suspension of the research pending a more thorough review (in accordance with procedures outlined in Section X of this policy)
6. The IRB sends written notification of determinations and actions taken to the PI/PD. Reports to other entities are made in accordance with procedures described in X(I).

D. Allegations and reports of Non-Compliance

All members of the WU community involved in human research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional policies governing the conduct of research involving human participants including but not limited to all applicable federal and state regulations, Washington University policies and procedures, including IRB policies, governing research and the conditions outlined in the IRB assurances document. The Executive Chair (or designee) will respond to allegations and reports of violations of regulations and policies related to human research according to the procedures described below. The Executive Chair (or designee) will self-identify conflicts of interest as defined in the Glossary and will not participate in the investigation or review if a conflict exists.

1. Reports of non-compliance or suspected non-compliance: Reports/allegations of non-compliance or suspected non-compliance may be submitted by a PI, research staff, HRPO staff, IRB members, the Human Subject Research Quality Assurance/Quality Improvement Committee, or a research participant. Such reports/allegations may be made to the HRPO office, to the Vice Chancellor for Research, through the anonymous WU Compliance hotline (314-362-4998), or

through other institutional offices. When human research-related reports/allegations are received by other offices, HRPO is notified promptly. Reports/allegations should include as much information as possible regarding the event(s) or action(s). The identity of the informer will be kept confidential unless he/she provides permission to disclose identifying information.

2. Handling allegations of non-compliance:

- a. The individual staff member who first learns of the event or action will gather all relevant information and then refer the situation to the Executive Chair (or designee) for further investigation.
- b. If the Executive Chair (or designee) determines that the allegation has no basis in fact, no further action will be taken under this Policy. If the Executive Chair (or designee) determines that the allegation involves noncompliance in fact, the remainder of this procedure for non-compliance is followed. If, in the course of handling the allegation of noncompliance, the Executive Chair (or designee) is unable to resolve whether the allegation has a basis in fact, the matter will be referred to the PARC for further investigation.
- c. If the PARC determines that the allegation has no basis in fact, no further action will be taken under this Policy. If the PARC determines that the allegation involves non-compliance in fact, the remainder of this procedure for a report of noncompliance is followed.

3. Handling reports of non-compliance:

- a. The individual staff member who first learns of the event or action will gather all relevant information and then refer the situation to the Executive Chair (or designee) for further investigation.
- b. Further investigation of the noncompliance will include contact with the PI/PD and, when appropriate, consultation with the Vice Chancellor for Research, the Office of General Counsel, Risk Management, or another institutional offices, as appropriate.
- c. PIs/PDs may voluntarily initiate suspension or termination of their research until the allegation or report of noncompliance has been investigated and resolved. If deemed necessary by the Executive Chair (or designee), the matter will be referred to the PARC for possible suspension or termination (as described in Section X(G)).
- d. Once the investigation has been completed, the Executive Chair (or designee) will make an initial determination regarding whether the non-compliance constitutes serious or continuing noncompliance.
 - i. If, after investigation, the Executive Chair (or designee) determines that the noncompliance is not serious or continuing non-compliance and the proposed corrective action plan is appropriate, the event and corrective action plan will be documented in the file. No further action is required.
 - ii. If the Executive Chair (or designee) determines that the noncompliance is not serious or continuing non-compliance, but the proposed action plan does not seem appropriate, the Executive Chair (or designee) may work with the PI/PD on a proposed corrective action plan. Once the plan is appropriate, the event and corrective action plan will be documented in the file. No further action is required.
 - iii. If the Executive Chair (or designee) determines that the noncompliance is not serious or continuing non-compliance but is unable to determine an appropriate proposed corrective action plan,

the report is referred and reviewed by the PARC for determination of an appropriate corrective action plan (as described in Section X(F).

- iv. If the Executive Chair (or designee) determines that the report of noncompliance represents serious or continuing noncompliance, the report is referred and reviewed by the PARC (as described in Section X(F).
- v. A report of all non-compliance will be presented to the PARC at the next regularly scheduled meeting.

E. Complaints and Concerns to the IRB

1. The PI/PD should work with the research participant to resolve any complaints. HRPO may be contacted for assistance or advice on how to resolve the complaint. All complaints should be reported at the time of continuing review unless an unanticipated problem involving risks to the participants or others or noncompliance is identified. If an unanticipated problem involving risks to participants or others or noncompliance is identified this should be reported in accordance with Section X(B).
2. The Executive Chair (or designee) will promptly handle and, if necessary, investigate all complaints and concerns received including those from PI/PDs and research participants.
3. Complaints and concerns may be reviewed by the Executive Chair (or designee) and referred to the Protocol Adherence Review Committee (PARC), a fully constituted committee, as required in Section X (C) and (D).
4. A report of all complaints and concerns resolved administratively will be reported to the PARC.
5. The Executive Chair (or designee) will self-identify conflicts of interest as defined in the Glossary and will not participate in the investigation or review if a conflict exists.

F. Review by the Protocol Adherence Review Committee (PARC)

1. The PARC is a duly established IRB that adheres to the membership and committee requirements described in Section V of this Policy. The Committee meets monthly or on an ad hoc basis (when necessary) to review:
 - a. Allegations or reports of serious or continuing non-compliance;
 - b. Reports of complaints, concerns, or noncompliance not resolved at the Executive Chair level;
 - c. Allegations of noncompliance where the veracity of the allegation cannot be resolved at the Executive Chair level.
2. Review of these items will take place only when a majority (one more than 50% of the full committee) of the Committee members are present, including at least one member whose primary concerns are in nonscientific areas. No official actions will be taken at a meeting where a majority of the members, including a non-scientist, are not present.⁶²
3. PARC meetings will take place with all participating members physically present unless circumstances warrant conducting a meeting via telephone conference call or using speakerphone under the conditions described in Section V(A)(4).
4. Items will be individually presented, discussed, and the proposed actions voted on at a convened meeting. All Committee members' votes will be deemed equal and no proxy votes (written or by telephone) will be considered.⁶³
5. The HRPO will assign one or two primary reviewers to each protocol. The Primary reviewer(s) will be assigned protocols based on related expertise. When

making reviewer assignments, the HRPO staff will take into consideration the vulnerable populations involved in the research and ensure at least one individual who has experience with this population is scheduled to be present at the meeting. Primary reviewers are responsible for conducting an in-depth review of all pertinent documentation (see below) and presenting the research at the convened committee meeting. Materials provided, as applicable, to the primary reviewer(s) are:

- a. The IRB application;
 - b. Full protocol;
 - c. Consent document(s);
 - d. Correspondence related to the allegation or report;
 - e. Description of any actions taken to date;
 - f. The Executive Chair's recommendation of further actions, sanctions, and reporting;
 - g. Grant application, Investigator's Brochure, questionnaires or surveys, recruitment materials (when relevant);
 - h. Other materials (determined by the Executive Chair on a case by case basis).
6. All other Committee members will receive the documents named above in Section X (F)(5).
7. In general, materials are made available (in either paper or electronic format) to Committee members five to seven days in advance of the meeting to allow adequate time for review. Urgent review procedures may be invoked only under unusual circumstances. This does not include urgency that is a result of negligence or delay on the part of the investigator or his/her staff to submit human subjects applications in a timely fashion. On occasion, however, an investigator is faced with an immediate deadline beyond his or her control. The materials are distributed as soon as possible to Committee members to allow sufficient time for review prior to the meeting.
8. After the PARC determines whether or not the event constitutes serious or continuing noncompliance, the PARC shall vote that one or more of the following actions are warranted:
- a. Serious or continuing noncompliance:
 - i. No action necessary;
 - ii. Suspension or termination of some or all research activities (as described in Section X(G) of this Policy);
 - iii. Continuing monitoring of the research or the consent process;
 - iv. Modification of the research protocol or the consent document/process;
 - v. Modification of the continuing review schedule;
 - vi. Notification or re-consenting of current participants;
 - vii. Referral to the Human Subject Research Quality Assurance/Quality Improvement Committee for study audit/monitoring;
 - viii. Referral to Research Integrity Officer (RIO) if the allegation involves intentional, serious, or continuing noncompliance;
 - ix. Referral to the Institutional Official (Vice Chancellor for Research) and Dean for determining and imposing additional sanctions such as formal reprimands or limitations on research activity or publications;
 - x. Other (as appropriate to the violation).
 - b. Complaints, concerns, noncompliance:
 - i. No action necessary;
 - ii. Suspension or termination of some or all research activities (as described in Section X(G) of this Policy);

- iii. Continuing monitoring of the research or the consent process;
 - iv. Modification of the research protocol or the consent document/process;
 - v. Modification of the continuing review schedule;
 - vi. Notification or re-consenting of current participants;
 - vii. Referral to the Human Subject Research Quality Assurance/Quality Improvement Committee for study audit/monitoring;
 - viii. Referral to the Research Integrity Officer (RIO);
 - ix. Referral to the Institutional Official (Vice Chancellor for Research) and Dean for determining and imposing additional sanctions such as formal reprimands or limitations on research activity or publications;
 - x. Other (as appropriate to the violation).
- c. Allegations of noncompliance: whether the noncompliance has a basis in fact:
- i. If not, no further action is taken under this Policy
 - ii. If yes, the matter is returned to the Executive Chair (or designee) under "Handling or reports of noncompliance."
9. The Committee's determination will be documented, in writing, via a letter from the Executive Chair (or designee) to the PI/PD and minutes will be recorded and distributed for committee approval as described in Section III(2) of this Policy.
10. Reports of unanticipated problems involving risks to participants or others, serious or continuing noncompliance, and suspensions or terminations will be reported to the appropriate regulatory agencies and appropriate institutional officials as described in Subsection I below.

G. Suspension and Termination

- 1. The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with IRB policies or that has been associated with unexpected serious harm to participants.⁶⁴
- 2. Any full board committee has the right to suspend or terminate research when provided with new information that warrants such action.
- 3. The Executive Chair or Executive Director may suspend research in situations where there is immediate risk of serious harm to participants. Such suspensions will be reported to the PARC at the next convened meeting.
- 4. When a suspension or termination occurs the IRB or person ordering the suspension or termination will consider
 - a. Actions to protect the rights and welfare of currently enrolled participants and whether or not to notify current participants of the suspension or termination.
 - b. whether procedures for withdrawal of enrolled participants take into account their rights and welfare.
- 5. Any adverse events or outcomes that result from a suspension or termination must be reported to the IRB.
- 6. Reports of suspensions and terminations will be generated and distributed by a member of the Compliance Review Team as detailed in Section X(I) of this Policy.
- 7. Suspensions and terminations cannot be overturned by Institutional Officials.

H. New Information

- 1. The Executive Chair (or designee) will review reports of new information that may impact the willingness of participants to participate or continue participation in the research study.

2. If the report of new information represents no more than a minimal risk of harm the event is acknowledged by the Executive Chair (or designee) along with requiring any additional actions as described in Section X(C)(5).
3. If the report of new information represents more than a minimal risk of harm the event will be reviewed by a fully convened committee.

I. Reporting

1. Reports of problems determined to represent unanticipated problems involving risks to participants or others, noncompliance determined to represent serious or continuing noncompliance, and suspensions and terminations of IRB approval will include:
 - a. The nature of the event.
 - b. Name of the institution conducting the research.
 - c. Title of the research project and/or grant proposal in which the problem occurred.
 - d. Name of the principal investigator on the protocol.
 - e. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement).
 - f. A detailed description of the problem or event including the findings of the IRB and the reasons for the IRB's decision.
 - g. Actions the institution is taking or plans to take to address the problem
 - h. Plans, if any, to send a follow-up or final report by the earlier of:
 - i. A specific date.
 - ii. When an investigation has been completed or a corrective action plan has been implemented.
2. Reports of problems determined to represent unanticipated problems involving risks to participants or others*, noncompliance determined to represent serious or continuing noncompliance, and suspensions and terminations of IRB approval will be distributed to :
 - a. OHRP (when the study is federally funded)
 - b. FDA (when the study is regulated by the FDA)
 - c. Vice Chancellor for Research (Institutional Official)

*For multicenter research projects, only the institution at which the participant(s) experienced an adverse event determined to be an unanticipated problem (or the institution at which any other type of unanticipated problem occurred) must report the event as described in X(I)(2) above.
3. When appropriate and applicable, copies of the report will be distributed to one or more of the following:
 - a. The Dean of the PI/PD's School;
 - b. The PI/PD's Department Chair, Division Chief/Program Director, or supervisor (if there is no department chair);
 - c. The investigator's Faculty Sponsor;
 - d. The appropriate WU sponsored research office (i.e., Grants & Contracts, Research Office) when the study is externally funded;
 - e. The Center for Clinical Studies, if the study is industry sponsored;
 - f. Human Subject Research Quality Assurance/Quality Improvement Committee;
 - g. Research Integrity Officer Office of Risk Management;
 - h. Office of General Counsel;

- i. Barnes-Jewish Hospital or Saint Louis Children's Hospital administrative representative;
 - j. The highest academic official of any other institution;
 - k. Study sponsor (including Industry Sponsors and Granting Agencies) when the PI/PD has not reported the event to the sponsor. (Reports may be made to the CRO representing the sponsor.) and/or;
 - l. Other federal agencies, when the research is overseen by those agencies and they require reporting separate from that to OHRP.
4. Determinations of unanticipated problems involving risks to participants or others, serious or continuing noncompliance or suspension or termination of previously approved research will be reported in writing or via email within 30 days of the final determination.
- a. Investigators may appeal a determination that an event represents an unanticipated problem, serious or continuing noncompliance, suspension or termination. The appeal must be received in writing within 14 days of the notice of the determination to the investigator. Appeals must contain new information that was not previously presented to the board and should not be simply a restatement of information already considered.
 - b. Appeals will be reviewed by the Compliance Review Team and if found to contain new information will be referred back to PARC.
 - c. If an appeal is referred back to PARC, reporting of the determination will occur within 30 days of the final PARC determination.

XI. HRPO Office

- A. HRPO physical office space includes adequate resources (meeting area, filing space, equipment, and computers) to support the IRB mission.
- B. HRPO staff
 1. The HRPO employs a sufficient number of staff members who are responsible for supporting and managing the IRB's review and record keeping duties for both the WU Medical School and Danforth campuses. Specific staff responsibilities are outlined in job descriptions on file in the HRPO office.
 2. HRPO staff have a description of the responsibilities expected of their positions and their performance is evaluated at least annually.
 3. In addition to the intensive training at the time of hire, HRPO staff members are provided and expected to participate in ongoing educational opportunities such as attendance at regional and national IRB conferences and HRPO sponsored events (i.e. bimonthly Question and Answer sessions, IRB retreats, and HRPO staff in-services).
 4. All staff members must pass the required CITI modules (<https://aisinfo.wustl.edu/ra.html>).
- C. IRB Chairs' Meeting
 1. The Chairs' meeting is comprised of the Executive Chair, alternate Chairs, representatives of the HRPO staff and WU General Counsel.
 2. Meetings will occur monthly to review and discuss selected issues that arise at the committee meetings or administrative level and to provide ongoing education to the Chairs.
- D. IRB Policies and Procedures
 1. HRPO will maintain and follow up-to-date policies and procedures that adhere to regulatory mandates and ethical principles.
 2. Changes to regulations, federal guidelines, institutional policy, or best research practices may require a new policy or a revision to the existing policy. Such new policies or revisions will be reviewed and approved by the Executive Chair and the Executive Director prior to implementation and will be documented in the appropriate policy and/or procedure manual.
 3. New policies or procedures or modifications to existing policies or procedures will be disseminated to the appropriate individuals and departments. When applicable, training for HRPO staff, IRB members, or the research community will be provided.
- E. HRPO Monitoring Functions
 1. The HRPO performs random consent audits on open protocols. The consent forms signed by the three most recently enrolled participants are reviewed to ensure compliance with regulatory and policy requirements.
 2. The HRPO monitors compliance with consent requirements by requiring that PI/PDs confirm that signed consent forms are on file for all participants at the time of continuing review.

3. HRPO staff conduct audits of full board minutes. Errors or omissions in audited minutes are noted and clarified in addendums to the minutes.
 4. The HRPO collaborates with the Human Subject Quality Improvement/Quality Assurance Program.
- F. The IRB is in compliance with the Washington University HIPAA policy as documented in the HRPO HIPAA Procedures.
- G. IRB Function in relation to other WU Committees/Offices: The IRB functions independently of, but in coordination with, the following Committees/Offices.
1. Office of General Counsel (OGC): The IRB and HRPO staff communicate regularly with committed members of the WU OGC on issues related to State and Federal law, interpretations of the regulations, and development of necessary agreements (e.g., IRB Authorization Agreements, Independent Investigator Agreements).
 2. Deans/Department Chairs: The Executive Chair and HRPO staff communicate with Deans/Department Chairs informally when responding to inquiries or recruiting new members and formally when reporting instances of noncompliance and at the Executive Chair's presentation for the WUSM Medical Executive Committee. Additionally, the Executive Chair may consult with Deans/Department Chairs regarding specific protocols if there are questions related to adequacy of resources, expertise, or other matters for which the School/Department has jurisdiction.
 3. Committee on Research Integrity (CRI): The CRI investigates allegations of research misconduct as defined in WU's Research Integrity Policy and includes "...knowing, serious or continuing violations of federal and institutional rules and regulations governing the conduct of research involving human participants..." The Executive Chair and behavioral subcommittee chair serve as *ex officio* members of the CRI.
 4. Alzheimer's Disease Research Center (ADRC): Protocols that involve participants, tissue, or data from the ADRC require the signature of the ADRC Executive Director (or named designee). IRB review and approval will not be held contingent upon ADRC approval.
 5. Antibiotics Utilization Review (AUR) Committee: Research involving administration of an FDA-approved antibiotic that is non-formulary or for which use is restricted at Barnes-Jewish Hospital requires review by the AUR Committee. The IRB will not review submissions requiring approval from the AUR until the AUR has reviewed and approved the protocol.
 6. Center for Clinical Studies (CCS): The HRPO office coordinates with the contract office within CCS to ensure that consent forms and contracts are consistent in regards to the terms of coverage in the event of a research-related injury.
 7. Conflict of Interest Review Committee (CIRC): The IRB relies on the CIRC to review, make recommendations, and, if applicable, manage financial conflicts of interest. In cases where the CIRC determines a financial interest requires management a written summary reflecting the CIRC's determination and (when applicable) a summary of the proposed management strategy is provided to the IRB for consideration by the full board or expedited reviewer. As part of the IRB review, the IRB has the authority to request additional actions to manage the conflict of interest to increase protection for research participants. If additional actions are requested this information will be

communicated to the CIRC. The IRB has the final authority to determine whether the research with the financial interest and the management plan, if any, allow the research to be approved. In addition, the Executive Chair and two IRB members have full membership status on the Medical School CIRC. The Chair of the Behavioral Subcommittee has full membership on the Danforth CIRC. At least one of these individuals will attend any full or sub-committee meetings involving review of a financial interest that may be related to human participant research.

8. Center for Applied Research Sciences (CARS): Research conducted at the CARS must be reviewed and approved by the (GCRC) General Clinical Research Center Advisory Committee (GAC) prior to initiating the research activity on CARS premises. CARS research protocols should be submitted to the GAC and the IRB simultaneously. IRB approval will not be held contingent upon GAC approval.
9. Embryonic Stem Cell Research Oversight Committee (ESCRO): The ESCRO provides oversight for investigators engaged in human embryonic stem cell research, assuring the responsible conduct of human embryonic stem cell research and compliance with federal, state, and local laws and regulations. Research involving the use of human embryonic stem cells requires approval by ESCRO prior to review by the IRB.
10. Human Subject Research Quality Assurance/Quality Improvement Committee (HSR QA/QI): The HSR QA/QI Committee monitors studies after IRB approval has been granted and research participants have been enrolled/recruited. The goal of the committee is to insure the safety of human research participants by monitoring compliance with the research protocol, WU policies, and federal regulations. The IRB may communicate any issues of concern to HSR QA/QI staff in order to request review of a particular study. Monitoring results of the HSR QA/QI Committee will be shared with the Executive Chair and Executive Director.
11. Institutional Biosafety Committee (IBC): Research involving the deliberate transfer of DNA (or DNA of RNA derived from recombinant DNA) into one or more human participants requires initial and continuing review by the IBC. The IRB will not review submissions requiring approval from the IBC until the IBC has reviewed and approved the protocol. SAEs that occur in these protocols require reporting to the IBC and the IRB. IRB approval of SAEs will be held contingent upon IBC approval. IBC approval will be documented in the protocol file.
12. Investigational Drug Service: Pharmacists dispensing investigational drugs for inpatient research protocols verify that the protocol has current IRB approval and that the patients signed an IRB-approved consent form prior to dispensing the drug. Copies of active IRB-approved protocols involving investigational drugs are available in the Pharmacy Department.
13. Joint Practice Committee of Children's Hospital: Research conducted in the Neonatal Intensive Care Unit (NICU) must be reviewed and approved by the Joint Practice Committee. IRB review and approval will not be held contingent on approval by the Joint Practice Committee.
14. Protocol Review and Monitoring Committee (PRMC): The PRMC is required by the National Cancer Institute to review all cancer-related research. Cancer-related new submissions, renewals, and modifications will be submitted to the PRMC for scientific review prior to IRB review. The IRB will

not approve submissions requiring approval from the PRMC without documentation of PRMC review and approval in the protocol file.

15. Pharmacy and Therapeutics (P&T) Committee: Research involving administration of an FDA-approved drug that is non-formulary or for which use is restricted at Barnes-Jewish Hospital requires review by the P&T Committee. The IRB will not approve submissions requiring approval from P&T without documentation of P&T review and approval in the protocol file.
16. Radiation Safety Committee (RSC): Research involving the administration of therapeutic radiation doses using sealed sources that the participant would not otherwise receive as part of his/her medical care requires review by the RSC. The IRB will not approve submissions requiring approval from the RSC without documentation of RSC review and approval in the protocol file.
17. Radioactive Drug Research Committee (RDRC): The RDRC is authorized by the FDA to approve research which involves the use of certain “non-approved” radioactive drugs for pre-Phase I research. The IRB will not approve submissions requiring approval from RDRC without documentation of RDRC review and approval in the protocol file.
18. The Center for Clinical Imaging Research (CCIR): The CCIR is a biomedical imaging facility that provides advanced imaging technology, equipment and expertise to support basic and translational inpatient and outpatient clinical research. Research conducted at the CCIR should be submitted for review by the CCIR Advisory panel. IRB approval will not be held contingent upon CCIR approval.
19. Quality Assurance and Safety Monitoring Committee (QASMC): QASMC reviews SAEs occurring on all cancer trials, data and safety monitoring reports on institutional cancer studies, and performs quality assurance audits on institutional therapeutic trials. QASMC notifies the IRB when their review results in protocol or consent form modifications.
20. Office of Sponsored Research Services (OSRS): OSRS establishes accounts in the WU financial system for extramural research awards. OSRS will only release funds for expenditure on research awards involving human research upon certification of IRB approval of the research. OSRS may freeze funds at any time during the sponsored project period, upon notification by the IRB of a PI/PD’s non-compliance with human participant research policies and procedures. Funds may continue to be frozen until the issue is resolved.
21. Office of Technology Management (OTM): The OTM manages a wide variety of intellectual properties arising from research programs throughout the University. These areas range from patents, copyrights, know-how, and proprietary materials. OTM assists faculty with consulting agreements and research contracts. HRPO works collaboratively with OTM with regard to transfer of materials that were collected as part of human subject research to ensure, when appropriate, that IRB approvals are in place and that the transfer is consistent with the approved protocol and consent documentation.

- H. HRPO Function in Relation to Regulatory Bodies and National Committees/Offices: The HRPO functions in compliance with OHRP and FDA requirements (as described in this document) and, additionally, adheres to the standards recognized by the Association for the Accreditation of Human Research Protection Programs (WU was accredited by AAHRPP 7/30/04; reaccreditation 9/14/07).

Glossary

Assent: A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as Assent.⁶⁵

Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.⁶⁶ In Missouri, individuals aged 18 or older are recognized as adults unless emancipated by adjudication, marriage, or pregnancy. (See Missouri Statute Chapter 211, Section 211.442-487; and Chapter 431, 431.065, Chapter 404, Section 404.410).

Clinical Investigation: "Any experiment that involves a test article and one or more human participants 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 21 CFR 58, regarding nonclinical laboratory studies."⁶⁷

Conflict of Interest in Research: A **financial conflict of interest** exists whenever a reviewer (including HRPO staff or consultants) or his/her immediate family (his/her spouse or dependent children):

1. has a financial interest in the research whose value cannot be readily determined;
2. has ownership interest, stock options, or other financial interests related to the research **UNLESS all** four of the following criteria are met:
 - a. does not exceed \$10,000 when aggregated for the immediate family;
 - b. is publicly traded on a stock exchange;
 - c. no arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research; **AND**
 - d. does not exceed 5% interest in any one single entity when aggregated for the immediate family.
3. has a significant financial interest with the sponsor of the study, the supporting organization, or the company that owns or licenses the technology being studied;
4. has received or will receive any compensation whose value may be affected by the outcome of the study;
5. has a proprietary interest in the research (property or other financial interest in the research including, but not limited to, a patent, trademark, copyright or licensing agreement);
6. has received payments from the sponsor that exceed \$10,000 per year;
7. is an executive or director of the agency/company sponsoring the research; or
8. any other situations defined by WU Conflict of Interest policies.

A **non-financial conflict of interest** exists whenever a reviewer (including HRPO staff or consultants) or his/her immediate family (spouse or dependent children) is:

1. the protocol director, or other member of the research team;
 2. listed on the FDA 1572 form or otherwise involved in the conduct of the study. (A conflict of interest does not exist if the reviewer is only providing a commercial service such as dispensing study medication or performing a blood draw);
 3. related to any member of the study team;
 4. the faculty advisor of the PI/PD;
 5. identified as "key personnel" on a funding mechanism that supports the research project;
- or

6. any other situation where the reviewer believes that another interest conflicts with his/her ability to deliberate objectively on a protocol.

Emergency Use: The use of a test article on a human participant in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

Engaged: The OHRP considers an institution to be engaged in human research when its employees or agents: (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes.

Exempt Category 2a: This category applies to non-federally funded research, conducted with competent adults, that would meet criteria for 45 CFR 46.101(b)(2) if an intervention were not involved. Exempt category 2a will allow exemption for those studies involving benign interventions or tasks beyond educational testes, surveys, focus groups, interviews and similar procedures that are commonly used in social and behavioral research and known to involve virtually no risk to participants.

Exculpatory Language: Please see <http://ohrp.osophs.HHS.gov/humansubjects/guidance/exculp.htm> for examples of exculpatory language.

Financial Interest: Any relationship entered into by any member of the study team, other than employment by Washington University (or the primary employment of non-WU collaborators), which could result in financial gain for the individual or his/her immediate family (i.e., spouse and dependent children).

Guardian: An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. In Missouri, a guardian is appointed by a juvenile or probate court which specifies the duties and responsibilities of such guardian. (See Missouri Statute Chapters 404, 453 and 475.)

Humanitarian Use Device: A device that the FDA has determined to benefit patients in treatment or diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the US per year.

Human Subject: In research regulated by HHS, a human subject is 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.⁶⁸ In FDA-regulated research, a human subject is defined as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control or, in the case of device research, an individual on whom or on whose specimen an investigational device is used or as a control.

Intervention: Physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.⁶⁹

Interaction: Communication or interpersonal contact between investigator and participant.⁷⁰

Legally authorized representative: An individual or judicial or other body authorized under applicable State law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research.⁷¹ (For research taking place in Missouri, see Missouri Statute Chapter 431, Section 431.064)

Life-Threatening: Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival.

Minimal risk: 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.⁷²

Minimal risk for research involving prisoners: The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.⁷³

Non-compliance: Failure to follow any applicable federal, state, WU, or IRB policies, procedures or regulations governing the conduct of research involving human participants, including but not limited to all applicable Federal and State regulations, Washington University policies and procedures governing research and the conditions outlined in the IRB assurances document (signed at the time of submitting a new protocol) and the IRB Policies and Procedures.

Non-scientist: Nurses, pharmacists and other biomedical health professionals are not regarded as having "primary concerns in the non-scientific area." Lawyers, clergy, ethicists, and social workers are examples of persons whose primary concerns would be in non-scientific areas. Members who have training in both scientific and non-scientific disciplines, such as a J.D., R.N. will not be appointed to satisfy the non-scientist requirement.⁷⁴

Non-significant risk device: A non-significant risk device is one that does not meet the definition for a significant risk device. Examples of non-significant risk devices include low power lasers for treatment of pain, daily wear contact lenses and associated lens care products not intended for use directly in the eye, Magnetic Resonance Imaging (MRI) devices within FDA specified parameters, Ob/Gyn diagnostic ultrasound within FDA approved parameters, wound dressings.⁷⁵

Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.⁷⁶

Private information: 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 participant 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 participants.⁷⁷

Protocol: The plan for a course of medical treatment or for a scientific experiment. A protocol should include the following components (when applicable): the study title, the purpose of the study, the sponsor, results of previous related research, participant inclusion/exclusion criteria, justification for use of any special/vulnerable participant population, study design, description of the procedures to be performed, provisions for managing adverse reactions, the circumstances surrounding consent procedure, the procedures for documentation of informed consent including any procedures for obtaining assent from minors, using witnesses, translators and document storage, compensation to participants for their participation, any compensation for injured research participants, provisions for protection of participant's privacy, extra costs to participants for their participation in the study, and extra costs to third party payers because of an individual's participation.⁷⁸ This information may be provided either in the protocol or in the IRB application.

Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.⁷⁹

Significant risk device: An investigational device that:

- (1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant;
- (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a participant;

(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a participant; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.⁸⁰

Suspension: A fully convened committee, the Executive Chair or Executive Director, may place a temporary halt to a selection of research activities, being conducted under an IRB-approved project or a temporary halt to the IRB-approved project as a whole.

Termination: A fully convened committee, may require a permanent halt to some or all research activities in a previously approved IRB project.

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- ¹ Federal Wide Assurance for the Protection for Human Subjects, Section A(1) (Version Date 3/20/02)
- ² Federal Wide Assurance for the Protection for Human Subjects, Section A(7) (Version Date 3/20/02)
- ³ 45 CFR 46.101(h) and 21 CFR 56.112
- ⁴ Federal Wide Assurance for the Protection for Human Subjects, Section A(5) (Version Date 3/20/02), 45 CFR 46.109(a)
- ⁵ Authority was delegated by Chancellor Wrighton in a May 1, 2004 memo to Drs. Philip Ludbrook and Sandra Hale. Delegation is also documented in the “Institutional Statement of Commitment to the Protection of Human Participants in Research at Washington University.”
- ⁶ 45 CFR 46.112
- ⁷ Archived Internal HRPO Policies (Version Date 3/12/01)
- ⁸ Federal Wide Assurance for the Protection for Human Subjects, Section A(9) (Version Date 3/20/02), 45 CFR 46.103(b)(2)
- ⁹ Federal Wide Assurance for the Protection for Human Subjects, Section A(2) (Version Date 3/20/02)
- ¹⁰ 45 CFR 46.114
- ¹¹ OHRP Guidance Document, “IRB Knowledge of Local Research Context” (Version Date 7/21/00)
- ¹² 21 CFR 812.3
- ¹³ Washington University Policy on Open Research and Free Dissemination of Ideas and Information
- ¹⁴ 45 CFR 46.115(a)(1), 21 CFR 56.115(a)(1), OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ¹⁵ 45 CFR 46.115(a)(2), 21 CFR 56.115(a)(2), OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ¹⁶ 45 CFR 46.115(a)(3), OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ¹⁷ 45 CFR 46.103(b)(3), 21 CFR 56.115(a)(5)
- ¹⁸ 45 CFR 46.103(b)(4-5), 21 CFR 56.108(a-b), OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ¹⁹ 45 CFR 46.115(b), 21 CFR 56.115(b)
- ²⁰ 45 CFR 46.107 (a-d), 21 CFR 56.107(a-e)
- ²¹ 45 CFR 46.107(a), 21 CFR 56.107(a), 45 CFR 46 Subpart C
- ²² 45 CFR 46.107(e), 21 CFR 56.107(e), OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ²³ 45 CFR 46.107(f), 21 CFR 56.107(f)
- ²⁴ Archived Internal HRPO Policies (Version Date 3/12/01)
- ²⁵ Archived Internal HRPO Policies (Version Date 3/12/01)
- ²⁶ 45 CFR 46.108(b), 21 CFR 56.108(c)
- ²⁷ In a 4/23/04 email from David Lepay (FDA) to Sarah Frankel, Ph.D. (HRPO), Dr. Lepay noted that while the regulations and the FDA do not explicitly require a physician to be present for the IRB to conduct business, “. . . it seems reasonable to assume that in most instances you would need the expertise provided by a physician in reaching a decision on the approvability of a protocol involving an investigational drug product.” However, Dr. Lepay stated, “We do not believe that FDA has ever taken a position on the various licenses given to physicians.” It is on the basis of this statement that the HRPO considers a Doctor of Chiropractic to meet the physician requirement.

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- ²⁸ OHRP Guidance Document, “IRB Meetings Convened via Telephone Conference Call” (Version Date 3/28/00)
- ²⁹ Archived Internal HRPO Policies (Version Date 3/12/01)
- ³⁰ OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ³¹ Archived Internal HRPO Policies (Version Date 3/12/01)
- ³² OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02), OHRP Guidance Document, “Local IRB Review of Multi-Center Clinical Trials” (Version Date 11/9/92)
- ³³ Archived Internal HRPO Policies (Version Date July 2008)
- ³⁴ OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ³⁵ FDA Information Sheet, “Recruiting Study Subjects”
- ³⁶ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ³⁷ Archived Internal HRPO Policies (Version Date July 2008)
- ³⁸ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ³⁹ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02) and FDA Information Sheet, “Continuing Review After Study Approval” (Version Date 1998)
- ⁴⁰ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ⁴¹ 45 CFR 46.110(b), 21 CFR 56.110(b)
- ⁴² 45 CFR 46.110(d), 21 CFR 56.110(d)
- ⁴³ Archived Internal HRPO Policies (Version Date July 2008)
- ⁴⁴ Archived Internal HRPO Policies (Version Date 3/12/01)
- ⁴⁵ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ⁴⁶ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02) and FDA Information Sheet, “Continuing Review After Study Approval” (Version Date 1998)
- ⁴⁷ OHRP Guidance Document, “Guidance on Continuing Review” (Version Date 7/11/02)
- ⁴⁸ FDA Information Sheet, “Recruiting Study Subjects”
- ⁴⁹ 45 CFR 46.116(a-b), 45 CFR 46.117(a-b), 21 CFR 50.25(a-b), 21 CFR 50.27(a-b)
- ⁵⁰ 45 CFR 46.116(d)(1-4)
- ⁵¹ Federal Register, Volume 61, No. 192, pp. 51531-51533
- ⁵² 45 CFR 46.117(c)(1-2)
- ⁵³ 45 CFR 46 Subpart B
- ⁵⁴ 45 CFR 46 Subpart C, OHRP Guidance Document “Approving Research Involving Prisoners” (Version Date 5/19/00)
- ⁵⁵ 45 CFR 46 Subpart D, OHRP Guidance Document “NIH Policy Guidance on the Inclusion of Children in Research” (Version Date 7/1/98)
- ⁵⁶ 21 CFR 812.66
- ⁵⁷ 21 CFR 50.23, 21 CFR 50.24, OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ⁵⁸ Federal Register, Volume 61, No. 192, pp. 51531-51533
- ⁵⁹ OHRP Guidance Document, “Informed Consent Requirements in Emergency Research” (Version Date 10/31/96)
- ⁶⁰ 21 CFR 814.124
- ⁶¹ OHRP Guidance Document, “OHRP Guidance on Written IRB Procedures” (Version Date 7/11/02)
- ⁶² 45 CFR 46.108(b), 21 CFR 56.108(c)
- ⁶³ Archived Internal HRPO Policies (Version Date 3/12/01)
- ⁶⁴ 45 CFR 46.113, 21 CFR 56.113
- ⁶⁵ 45 CFR 46.402(b)

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- ⁶⁶ 45 CFR 46.402(a)
 - ⁶⁷ 21 CFR 50.3(c)
 - ⁶⁸ 45 CFR 46.102(f)
 - ⁶⁹ 45 CFR 46.102(f)
 - ⁷⁰ 45 CFR 46.102(f)
 - ⁷¹ 45 CFR 46.102(c), 21 CFR 50.3(l)
 - ⁷² 45 CFR 46.102(i), 21 CFR 50.3(k)
 - ⁷³ 45 CFR 46.303(d), 21 CFR 50.3 (o)
 - ⁷⁴ FDA Information Sheet, "IRB Membership"
 - ⁷⁵ FDA Information Sheet, "Medical Devices"
 - ⁷⁶ 45 CFR 46.303(c)
 - ⁷⁷ 45 CFR 46.102(f)
 - ⁷⁸ FDA Information Sheets, A self-evaluation checklist for IRBs
 - ⁷⁹ 45 CFR 46.102(d)
 - ⁸⁰ 21 CFR 812.3(m)