



**Department of Veterans Affairs
Jesse Brown VA Medical Center
820 S. Damen Avenue
Chicago, IL. 60612**

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SOP: JBVAMC Human Subjects Protection Program (HSPP)

POLICY:

The Medical Center Director is ultimately responsible for the development and implementation of the JBVAMC HSPP Plan and the coordination of all its components.

JBVAMC HSPP MISSION:

The mission of the JBVAMC HSPP is to ensure that there are mechanisms developed and maintained to ensure an effective HSPP, which in turn should ensure the protection of the rights and welfare of all human subjects involved in research.

I. DEFINITIONS

(1) **Accreditation.** Accreditation of a Human Subjects Protection Program (HSPP) is the process of obtaining independent recognition that a HSPP affords protection to human subjects by meeting and exceeding the prevailing ethical, professional, and regulatory requirements, and that the HSPP engages in continuous quality improvement.

(2) **Anonymous.** For the purposes of VA research, anonymous means de-identified in accordance with both: (1) The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 CFR 164.514(b) (see VHA Handbook 1605.1), and (2) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or associated with the information (38 CFR 16.102(f)).

(3) **Assurance (Assurance of Compliance).** For human research, an Assurance is a written commitment to protect human subjects participating in research and to comply with the requirements of 38 CFR Part 16. Assurances are reviewed and approved by the HHS Office for Human Research Protections (OHRP) and various other departments and agencies under the Federal Policy (Common Rule) for the Protection of Human Subjects (56 FR 28001, June 18, 1991) (see VHA Handbook 1058.03). **NOTE:** For the purposes of VHA Handbook 1200.05, the terms *Assurance*, *Assurance of Compliance*, and *Federalwide Assurance (FWA)* are *synonymous*.

(4) **Case Report.** A case report is medical information collected and presented on one (1) patient to highlight an interesting treatment, presentation, or outcome. A case report generally results

from a retrospective review of the medical record and/or the clinical provider's files. In this regard, case reports differ from research protocols in which data are collected with intent to evaluate a specific hypothesis.

(5) **Clinical Investigation.** As explained in VHA Handbook 1200.05, the FDA considers the term clinical investigation to mean any experiment that involves a test article and one or more human subjects, and that either: (1) Meets the requirements for prior submission to the FDA under § 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act; or (2) Does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

(6) **Coded Data.** The term "coded data" means "coded private information" as defined in guidance published by HHS entitled Guidance on Research Involving Coded Private Information or Biological Specimens, currently available at:
<http://www.dhhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>

(7) **Credentialing.** Credentialing is the systematic process of screening and evaluating qualifications and other credentials, including licensure, education, training, and experience, and current competence and health status (see VHA Handbook 1100.19).

(8) **Data.** The term data means information derived directly from patients or human research subjects or indirectly through accessing databases. It includes information from Deoxyribonucleic Acid (DNA) sequencing. It does not include information derived from research involving animals or other types of research that do not involve human subjects.

(9) **Data Repository.** A data repository is a database or a collection of databases that have been created or organized to facilitate the conduct of multiple research protocols, including future protocols not yet envisioned. It also may have been created for other purposes such as administrative and clinical purposes (VHA Handbook 1200.12). Data repository and data warehouse are interchangeable terms.

(10) **Database.** A database is a collection of data or information elements organized in a manner to permit systematic retrieval.

(11) **De-Identified Data.** (1) For the purposes of VA research, de-identified data are data that have been de-identified in accordance with both: (a) The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 CFR 164.514(b) (see VHA Handbook 1605.1), and (b) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or be associated with the information (38 CFR 16.102(f)). (2) Such data may also be known as "anonymous." **NOTE:** *Coded data is data identifiable by the individual(s) who has access to the code. Therefore, coded data are not considered to be de-identified or anonymous.*

(12) **Generalizable Knowledge.** Is relevant, useful and important information that attempts to make comparisons or draw conclusions from the gathered data, attempts to understand the principles of historical or social development, or seeks the underlying principles of laws of nature. It has predictive value and can be applied to other circumstances.

(13) **Human Biological Specimens.** Human biological specimens are defined as materials derived from human individuals, such as blood, urine, tissue, organs, hair, nail clippings, buccal

swabs, or any other materials that are either collected specifically for research purposes or as residual specimens from diagnostic, therapeutic, or surgical procedures. Bacteria, fungi, or viruses obtained from human biological specimens are not considered human biological specimens, as long as the human material has been removed.

(14) **Human Research.** Human research is research involving 1) human subjects, as defined by VHA Handbook 1200.05, 38CFR16, 45CFR46 and 21CFR50, or 2) one or more identifiable human biological specimens.

(15) **Human Subjects Protection Program (HSPP).** A HSPP is a comprehensive system to ensure the protection of human subjects participating in research. At the JBVAMC, the HSPP consists of a variety of individuals and committees including, but not limited to: the VA Medical Center Director, Associate Chief of Staff (ACOS) for R&D, Administrative Officer (AO) for R&D, Research Compliance Officer (RCO), R&D Committee, IRB, other committees or subcommittees addressing human subjects protection (e.g., Subcommittee on Research Safety (SRS), Institutional Biosafety Committee, Radiation Safety Committee, Conflict of Interest Committee), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

(16) **Human Subject.** A living individual about whom an investigator conducting research obtains either: (a) Data through intervention or interaction with the individual; interaction includes communication or interpersonal contact between the researchers and the subject; or (b) Identifiable private information (38 CFR 16.102 (f)). For research covered by Food and Drug Administration (FDA) regulations, human subjects means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. (21 CFR 50.3(g), 21 CFR 66.102(c)). For research covered by FDA device regulations, subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease (21 CFR 812.3(p)). The VA definition of human subject extends to investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled (VHA Handbook 1200.05).

(17) **Intervention.** Intervention includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes (38 CFR 16.102(f)(2)). Interventional studies are those in which the research subjects are assigned by the investigator to a treatment or other intervention, and their outcomes are measured.

(18) **Investigational Device.** As defined by the FDA, an investigational device is a device that is the object of an investigation (21 CFR 812.3(g)).

(19) **Investigational Device Exemption (IDE).** An IDE is an application to FDA that allows an investigational significant risk device to be used in a clinical investigation to collect safety and effectiveness data. If the device is a non-significant risk device, it is considered to have an approved application for IDE after IRB approval is obtained (see 21 CFR 812).

(20) **Investigational Drug.** According to VHA Handbook 1108.04, an investigational drug is a chemical or biological drug that is used in a clinical investigation. An investigational drug can be: (1) A new chemical compound, which has not been released by the FDA for general use; or (2)

An approved drug that is being studied for an approved or unapproved use, dose, dosage form, administration schedule, or under an Investigational New Drug (IND) application, in a controlled, randomized, or blinded study (see VHA Handbook 1108.04). **NOTE:** *Concurrent medications, comparators, or rescue medications used in the investigational trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels. Prescription drugs, over-the-counter drugs, nutritional supplements, herbal preparations, and legend items used for diagnosis or treatment and meeting the definition of “investigational drug” are considered investigational drugs.*

(21) **Investigator.** An investigator is any individual who conducts research involving human subjects including, but not limited to, the PI, co-PI, and Local Site Investigator (LSI). The investigator must uphold professional and ethical standards and practices, adhere to all applicable Federal requirements, and comply with applicable local policies and procedures.

(22) **Minimal Risk.** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (38 CFR 16.102(i)).

(23) **Observational Studies.** Observational studies are non-interventional studies in which individuals are observed and those observations are recorded. Outcomes, including health outcomes, may also be measured by the investigators.

(24) **Pilot Studies.** Pilot studies are full-fledged research studies that must be approved by the IRB(s), when human subjects are involved. They are not considered to be activities preparatory to research.

(25) **Preparatory to Research.** Within VHA, activities “preparatory to research” refer to activities that are necessary for the development of a specific protocol. PHI from data repositories or medical records may be reviewed during this process without IRB approval, subject authorization, or a waiver of authorization, but only aggregate data may be recorded and used in the protocol application (e.g., potential number of subjects meeting study criteria at each site). Within VHA, an activity preparatory to research does not include the identification of potential subjects and recording of data for the purpose of recruiting these subjects or to link with other data. The preparatory to research activity ends once the protocol has been submitted to the IRB for review.

(26) **Privacy Board.** Under HIPAA, a Privacy Board is a board that is established to review and approve requests for waivers or alterations of HIPAA authorizations in connection with use or disclosure of PHI. The Privacy Board:

- (1) Consists of members with varying backgrounds and appropriate professional competency, as necessary, to review the effect of the research protocol on the individual’s privacy rights and related interests;
- (2) Includes at least one member who is not affiliated with the covered entity, not affiliated with any entity conducting or sponsoring the research, and not related to any person who is affiliated with any of such entities; and
- (3) Does not have any member participating in a review of any study in which the member has a conflict of interest.

(27) **Private Information**

- (1) Private information must be individually identifiable in order for the information to constitute research involving human subjects.
- (2) Private information includes:

- (a) Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and
- (b) Information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record).

(28) **Research.** Research means a systematic investigation including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge.

(29) **Research and Development.** Research and Development in the VA includes the investigation and refinement of biomedical hypotheses related to human health, diseases, defects, and handicaps, and the treatment of these as well as the systematic study and refinement of problems and hypotheses related to the delivery of health care.

(30) **Research Involving Human Subjects.** Any activity that either a). meets the DHHS definition of “research” and involves “human subjects” as defined by DHHS; or b). meets the FDA definition of “research” (i.e., systemic investigation) and involves “human subjects” as defined by FDA.

(31) **Systematic Investigation.** An organized approach to develop new knowledge. It is planned and follows a definite set of steps and procedures. Generally, there must be a relevant question or hypothesis to be tested and use of a scientific method.

(32) **VA Investigator.** A VA investigator is any individual who conducts research approved by the VA R&D committee while acting under a VA appointment on VA time, including full and part-time employees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970.

(33) **VA Research.** VA research is research that is approved by the R&D Committee and conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments), utilizing VA resources (e.g., equipment), or on VA property including space leased to, and used by VA. The research may be funded by VA, by other sponsors, or be unfunded. **NOTE:** *Research conducted by non-VA investigators that does not utilize VA resources and that occurs on space, or with equipment, leased from VA or covered under a use agreement between VA and a non-VA entity is not considered VA research.*

VA International Research. VA international research is defined as any VA-approved research conducted at international sites (not within the U.S., its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research that entails sending such specimens or data out of the U.S. **NOTE:** *Research conducted by non-VA investigators that does not utilize VA resources and that occurs on space, or with equipment, leased from VA or covered under a use agreement between VA and a non-VA entity is not considered VA research.*

(34) **VA Sensitive Information.** (1) VA sensitive information is all department data, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the information. (2) The term includes information whose improper use or disclosure could adversely affect the ability of an agency to accomplish its mission; proprietary information; records about specific individuals requiring protection under various confidentiality provisions, such as the Privacy Act and the HIPAA Privacy Rule; and information that can be withheld under the Freedom of

Information Act.

II. Research Overseen by the JBVAMC's HSPP.

A. Research conducted at JBVAMC and overseen by the HSPP includes research involving human subjects according to DHHS, FDA, and VA regulations and human biological specimens.

B. External IRBs, the JBVAMC/Northwestern University/University of Illinois at Chicago Collaborative IRB (referred to as UIC IRB#4) and the VA Central IRB, review biomedical and social behavioral research and research involving all phases of clinical trials for both drugs and devices. The Collaborative IRB is comprised of three institutions, JBVAMC, NU, and UIC, who have agreed to rely on a single IRB with the authority to review biomedical and behavioral research that utilizes the JBVAMC as a recruitment and/or performance site. For more information, refer to the *Operating and Coordinating Procedures for the Administration of the Collaborative JBVAMC/NU/UIC IRB (UIC IRB #4)*. The VA Central IRB reviews the VA Cooperative Group studies. For more information, refer to the *SOP: Use of the VA Central IRB* for more information. The JBVAMC is not permitted to use a commercial IRB for review of VA research.

C. Participants in research include patients, healthy volunteers, federally defined vulnerable populations, the decisionally impaired, students, employees, and/or members of the community.

D. Classified research involving human subjects cannot be approved by the Collaborative IRB, the VA Central IRB or R&D Committee or performed at a VA facility, including space leased to and used by VA.

E. Planned emergency research must not be granted approval by the Collaborative IRB, the VA Central IRB or R&D Committee and cannot be conducted by VA. Patients receiving a test article in an emergency use that is regulated by FDA is not considered to be involved in research and is not a research subject. VA regulations pertaining to research involving human subjects do not permit data obtained from patients to be classified as human subjects research, nor may the outcome of such care be included in any report of a research activity subject to VA regulations pertaining to research involving human subjects.

F. When FDA-regulated products are used, FDA regulations apply regardless of funding source.

G. The Medical Center Director, or designee, must obtain permission from the CRADO prior to creating a new human research program and applying through VHA Office of Research Oversight (ORO) to OHRP for an FWA.

H. For research involving stem cells or cord blood, investigators should contact ORD for requirements.

I. Limits on Human Subjects Research at the JBVAMC

Research that is not permitted at the JBVAMC includes:

1. Research related to *in vitro* fertilization
2. Research using prisoners as subjects*
3. Research using children as subjects*
4. Research involving neonates or fetuses

(*The prohibitions on research with children or prisoners may be waived by special dispensation from VA Central Office. *In vitro* and embryonic stem cell prohibitions cannot be waived.)

Some research may be considered to be of questionable appropriateness to the JBVAMC:

1. Research whose sole purpose is to help students fulfill degree requirements
2. Projects which are unlikely to contribute to general knowledge
3. Research that would unduly strain the patient care mission of the JBVAMC or unduly inconvenience or embarrass VA patients
4. Research that would consume inordinate amounts of VA resources

J. Research Involving Prisoners

1. Research involving prisoners cannot be conducted by JBVAMC investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. If such a waiver is granted by the CRADO, the research must be in accordance with applicable Federal regulations pertaining to prisoners as research subjects (see UIC (Collaborative IRB) policy: **Research Involving Prisoners**). Requirements for requesting a waiver may be obtained by contacting ORD.
2. Incarceration During a Study. If a subject becomes incarcerated during the course of a study:
 - a. Investigators must notify the IRB as soon as they become aware that the subject has been incarcerated.
 - b. The investigator must make a determination as to whether or not it is the best interests of the subject to remain in the study, or if the subject can be safely withdrawn from the study.
 - c. If the investigator determines it is in the best interest of the subject to remain in the study, the subject's continued participation in the study is contingent on the IRB's reviewing and approving such participation. The IRB approval must comply with 45 CFR 46.301-306.
 - d. After IRB and other relevant approvals (e.g., from the penal system) for the incarcerated subject's continued participation in the study have been obtained, a waiver must also be obtained from the CRADO (see subpar. 47b).
 - e. Investigator must comply with all applicable requirements including, but not limited to, applicable court, penal system, and local, VA, and other Federal requirements.

K. Research Involving Children

1. Research involving children cannot be conducted by JBVAMC investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. Research involving biological specimens or data obtained from children is considered to be research involving children.
2. Prior to requesting a waiver, the following criteria must be met:
 - a. The study represents no greater than minimal risk as determined by the IRB.

- b. The study meets all requirements in 45 CFR 46, Subpart D, Additional Protections for Children Involved as Subjects in Research, Sections 46.401 through 46.404, and 46.408.
 - c. The IRB reviewing the study has appropriate membership to represent children's interests and pediatric expertise.
 - d. The IRB reviewing the study has specific SOPs regarding children in research.
 - e. The VA facility Director certifies that the facility is able to respond to pediatric emergencies if the study includes interactions with children at the VA facility.
 - f. If the sponsor of the research is not VA, the facility Director makes certain that the sponsor of the research has procured appropriate liability insurance.
3. Waiver Application. To request a waiver, the following information must be submitted to ORD for each protocol:
- a. A cover letter signed by the VA facility Director that contains the following information:
 - (1). Certification by the VA facility Director that the facility is able to respond to pediatric emergencies if the study includes an interaction with children at the VA facility.
 - (2). Any additional safeguards that have been incorporated into the clinical site where children will be studied.
 - (3). Information on the study's funding source and on liability coverage if the sponsor is not VA.
 - (4). Certification that the IRB has determined the study to be of no greater than minimal risk and has approved the study.
 - (5). A statement that the required elements of 45 CFR 46 Subpart D have been met.
 - (6). A description of the relevance to Veterans' health of both the study and the inclusion of children in the study.
 - b. A copy of the study protocol, the informed consent form, the assent document, and HIPAA authorization. The informed consent document signed by the parent or guardian is the vehicle for parent or guardian permission. Provisions for permission by parents or guardians must be documented in accordance with and to the extent required by 38 CFR 16.117.
 - c. Minutes of the IRB meeting approving the study. The IRB minutes need to reflect the discussion regarding level of risk, the informed consent and assent forms, the investigators' qualifications to conduct research involving children, and any additional safeguards incorporated into the protocol.
 - d. If the study involves biological specimens or data collected from children, in addition to the preceding requirements, the following must be submitted:
 - (1) A discussion of how the biological specimens or data were, or will be, obtained and under what consents or authorization.
 - (2) If the biological specimens or data were, or will be, collected for research purposes, the IRB approval, the informed consent form, and the HIPAA authorization for the research.
 - (3) If biological specimens or data were, or will be, collected from an international site, a waiver from the CRADO for international research (see par. 54).
 - (4) Plans for future use of biological specimens or data.

L. Research Involving Persons Who Lack Decision-Making Capacity

1. Persons who lack decision-making capacity are not to be subjects in research simply because they are readily available.
2. No individual who lacks decision-making capacity may participate in VA Research until the IRB has reviewed and approved that individual's, or that class of individuals', participation in a given study.
3. Criteria for Decision-Making Capacity
 - a. An individual is presumed to have decision-making capacity unless any one or more of the following apply:
 - (1) It has been documented by a qualified practitioner in the individual's medical record in a signed and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study. **NOTE:** *The qualified practitioner may be a member of the research team.*
 - (2) The individual has been ruled incompetent by a court of law.
 - b. If there is any question as to whether or not a potential adult subject has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision-making capacity, and the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the research team) about the individual's decision-making capacity before proceeding with the informed consent process.
4. Temporary or Fluctuating Lack of Decision-Making Capacity. Individuals, who because of a known condition, are at high risk for temporary (e.g., head trauma) or fluctuating (e.g., schizophrenia) lack of decision-making capacity must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual's ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a legally authorized representative (LAR) must provide informed consent. If the subject regains decision-making capacity, the investigator or designee must repeat the informed consent process with the subject, and obtain the subject's permission to continue with the study.
5. Criteria for Enrollment. Individuals who lack decision-making capacity may be enrolled in protocols if:
 - a. The proposed research entails:
 - (1) No greater than minimal risk to the subject as determined by the IRB; or
 - (2) If the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject or
 - (3) Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition.
 - b. The disorder (e.g., Alzheimer's) leading to the individual's lack of decision-making capacity is being studied, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke), but only if the study cannot be performed with only persons who have decision-making capability.
 - c. The subject of the study is not directly related to the individual's lack of decision-making capacity, but the investigator can make a compelling argument for including individuals who lack decision-making capacity in the study (e.g., transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in a nursing home

where both individuals with, and those without, decision-making capacity are affected).

6. IRB Determination. If the criteria in 5. above are met, the IRB may approve the inclusion of individuals who lack decision-making capacity in research studies on the basis of informed consent from LARs as described in 7. below.
 - a. Before approving the study, the IRB must:
 - (1) Ensure the study includes appropriate procedures for respecting dissent;
 - (2) Consider whether or not the study needs to include procedures for obtaining assent; and
 - (3) Determine whether any additional safeguards need to be used (e.g., consent monitoring).
 - b. The IRB must document its deliberations and the criteria in subparagraph 49d it used to approve inclusion of individuals who lack decision-making capacity in the IRB minutes or IRB protocol file.

7. Surrogate Consent

- a. Investigators' Responsibilities for Surrogate Consent. Investigators must:
 - (1) Provide the IRB with a description of the procedures to ensure that subjects' LARs are well informed regarding their roles and obligations to protect persons who lack decision-making capacity.
 - (2) Provide information (i.e., informed consent process and HIPAA authorization) to the subjects' LARs that would ordinarily be required to be made to the subjects themselves if they had decision-making capacity.
- b. LARs
 - (1) **Authorized Person.** The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority (38 CFR 17.32(e)):
 - (a) Health care agent (i.e., an individual named by the individual in a Durable Power of Attorney for Health Care (38 CFR.17.32(a)(iii));
 - (b) Legal guardian or special guardian;
 - (c) Next of kin in this order: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or
 - (d) Close friend.
 - (2) Responsibilities of LARs. LARs are acting on behalf of the potential subjects, therefore:
 - (a) LARs must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision.
 - (b) If the potential subject's wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects' best interests.
 - (c) LARs generally assume the same rights and responsibilities as the individuals who lack decision-making capacity in the informed consent process.
- c. Dissent or Assent. If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Although unable to provide informed consent, some persons may resist participating in a research (i.e., if they dissent) protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

M. Student And Other Trainee Research

Research Conducted by Students and Other Trainees to Fulfill Academic Requirements.

Only students and other trainees (including residents and fellows), including VA employees, from schools with an academic affiliation agreement (currently UIC and NU) consistent with current JBVAMC policy, may serve as investigators within JBVAMC, or use data, or human biological specimens that have been collected within JBVAMC for clinical, administrative, or research purposes. *A waiver may be obtained from the CRADO under special circumstances.*

A JBVAMC investigator sufficiently experienced in the area of the trainee's research interest must serve as PI or co-PI and is responsible for oversight of the research and the trainee. The PI or co-PI is responsible for ensuring the trainee complies with all applicable local, VA and other Federal requirements.

III. Ethical Principles.

The JBVAMC HSPP is guided by the ethical principles regarding all research involving humans as subjects as set forth in the Belmont Report "Ethical Principles and Guidelines for the Protection of Human Subjects of Research,"

<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm> regardless of who conducts the research or the source of support. The VA also follows the principals outlined in the Nuremberg Code and the "Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects". VA is one of the seventeen Federal departments and agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects (Common Rule), effective June 18, 1991.

1. VHA employees conducting or reviewing research are subject to the Federal Criminal Code and the Standards of Ethical Conduct for Executive Branch Employees, as well as the principles of the Belmont Report. The obligation to act in accordance with ethics laws and regulations applies to all individuals while acting under a VA appointment, including full and part-time employees, without compensation employees, and employees under the Intergovernmental Personnel Act of 1970. Ethics officials in the Office of General Counsel to in the VA Central Office and VA Regional Counsel Offices are available to provide guidance on dealing with actual or potential conflict of interest issues of all members of the local research team in accordance with their respective policies and standard operating procedures. (Source: JBVAMC – Central VA IRB MOU, p. 2).

2. UIC employees, independent contractors, and students must follow the respective UIC ethical policy and the general UIC mission and values, as well as the principles of the Belmont Report.

3. All IRB members and staff will receive appropriate initial and ongoing training with regard to VA and other Federal requirements for the protection of human subjects.

The JBVAMC R&D Office and the UIC OPRS work together to ensure that all policies and procedures are up to date, are available to all investigators via the UIC OPRS website, and that investigators are notified of policy and procedure changes via email notifications, the UIC OPRS newsletter, and the UIC OPRS website.

If a member of the R&D Office, UIC OPRS, IRB, or other member of the JBVAMC research community identifies a need for a policy and/or procedure change, the JBVAMC AO will be notified. The AO will work with the applicable R&D Office staff member to initiate the change and when applicable, the UIC OPRS staff will assist in revising any policies and/or procedures. Once the changes are made, the revised policy and procedure will be sent to the JBVAMC ACOS for R&D for review. All policy and procedure changes must contain the signature of the JBVAMC ACOS for R&D. Once the policy and procedures are approved by the JBVAMC ACOS for R&D, they will be sent to the UIC VA Liaison, who will communicate the policy change to the OVCR Communication Team Liaison for posting to the UIC OPRS website. When a policy and/or procedure change involving the RCO is necessary, the revised policy and procedure will require the signature of the Medical Center Director before posting to the UIC OPRS website via the VA Liaison and the OVCR Communication Team Liaison. Once the revised policy and procedures are posted to the UIC OPRS website, the VA investigators and research community will be notified via email by the R&D Office. In addition, the UIC OPRS website will include a notice and the policy and procedure change may be included in the following UIC OPRS Newsletter depending upon the nature of the change.

Research at the JBVAMC is covered by the following Federalwide Assurances (FWA):

1. UIC-IRB # 4 (#FWA 00000083)
2. Jesse Brown VAMC (# FWA 00000290)
3. VA Central IRB #1 (# FWA 00013518)

These FWAs reflect agreements between the JBVAMC, the University of Illinois at Chicago, and the VA Central IRB, Washington DC, the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP), and the Department of Veterans Affairs Office of Research Oversight (VA ORO). The agreements are designed to support the HSPP and are built on the assumption that the JBVAMC as an institution is accountable for and committed to the protection of human research subjects when engaging in its research mission.

The assurances formalize the JBVAMC commitment to protect human subjects participating in research. These agreements state that the JBVAMC is responsible for compliance with human research protection regulations as described in the Federal Policy for the Protection of Human Subjects, known as the Common Rule (including Subparts A, B, C, and D), and is guided by the ethical principles found in the Belmont Report (Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research). The assurances grant the JBVAMC the authority to hire or appoint, train, supervise, and discipline investigators.

The FWAs document the JBVAMC is responsible for assuring the scientific merit of research conducted within the institution and for assuring that human research subjects are protected. The FWAs state that the JBVAMC shall utilize the Health Sciences IRBs in the review of human research protocols. The IRBs, in turn, assure that the research protocols adequately protect human subjects and meet regulatory requirements. The JBVAMC, as part of this assurance function, conducts reviews of compliance and monitors and encourages quality improvement of its HSPP functions. In short, this facility shall operate a comprehensive and organized system to protect those who participate as subjects in its research.

The Medical Center Director is the institutional official (IO) responsible for maintaining the assurance. The Research and Development (R&D) Committee, in cooperation with the director, is responsible for ensuring that the HSPP is operational.

The arrangement concerning the Collaborative IRB is formalized and each institution's responsibility outlined in a memorandum of understanding (MOU) between UIC and the JBVAMC and an authorization agreement between UIC and Northwestern (NU), another JBVAMC affiliate. In addition, the JBVAMC also has an MOU with the Veterans Health Administration Central Office which outlines each institution's responsibilities. The VHA Central Office operates the VA Central IRB.

IV. Engaged / Not Engaged in VA Research.

A. Engaged in VA Research. JBVAMC is considered "engaged" in a particular non-exempt human subjects research study when an individual with a VA appointment (including full and part-time employees, WOC employees, and employees under the IPA of 1970) at that facility obtains for the purposes of the research study:

(1) Data about the subjects of the research through intervention or interaction with them; (2) Identifiable private information about the subjects of the research; or (3) The informed consent of human subjects for the research.

Note: When a VA facility is engaged in human subject research, it must:

- (1) Hold an FWA;
- (2) Have a VA PI or LSI for that study; and
- (3) Have the facility's IRB of record approve the study.

B. Not Engaged in VA Research

- a. If a VA facility is not engaged in any human research then the VA facility does not need to have an FWA.
- b. If a VA facility is not engaged in research for the purposes of an individual study, then its IRB of record does not need to approve that study.
- c. If a VA facility is not engaged in research for the purposes of a given study, it has no jurisdiction over that study, except the Medical Center Director may determine that the study cannot be conducted on its premises.

Refer to *OHRP Guidance on Engagement of Institutions in Human Subjects Research*, dated October 16, 2008, for examples and additional guidance. Please note that the UIC policy *Engaged or Not Engaged in Research* also discusses the issue of engagement.

V. IRB Authority: Affiliate IRB and VA Central IRB

The Collaborative IRB and VA Central IRB have the authority:

1. To review submissions that fall within the scope of research described above
2. To approve, require modifications to secure approval, and disapprove all research activities as indicated in the applicable MOU, UIC Policy *Operating and Coordinating Procedures for the Administration of the Collaborative JBVAMC/NU/UIC IRB (UIC IRB #4)*, and VA Central IRB SOP 101 *VA Central Institutional Review Board (IRB) Authority, Responsibilities and Activities*.
3. The JBVAMC Research and Development Committee has delegated the review of research for scientific validity to the Collaborative *JBVAMC/NU/UIC IRB (UIC IRB #4)*.
4. To suspend or terminate IRB approval of research not being conducted in accordance with the IRBs requirements or that had been associated with unexpected serious harm to subjects, as indicated in the applicable MOU, UIC Policy *Operating and Coordinating Procedures for the Administration of the Collaborative JBVAMC/NU/UIC IRB (UIC IRB #4)*,

and VA Central IRB SOP 101 *VA Central Institutional Review Board (IRB) Authority, Responsibilities and Activities*.

5. To observe, or have a third party observe, the consent process and the conduct of research as indicated in the UIC Policy *IRB Observation: Informed Consent Process/Ombudsman*, and VA Central IRB SOP 101 *VA Central Institutional Review Board (IRB) Authority, Responsibilities and Activities*.

The JBVAMC R&D Office ensures that research involving human subjects does not commence until the research has received all of the required approvals. Examples of the required approvals include, but are not limited to: applicable IRB approval, final Information Security Officer (ISO) review, and final Privacy Officer review. The JBVAMC Medical Administration Specialist does not forward the submission for review by the ACOS for R&D and/or the R&D Committee until after all approvals have been obtained. The Medical Administration Specialist forwards the written ACOS for R&D approval to the UIC VA Liaison for research reviewed and approved by the Collaborative IRB. As VA research may not be implemented until after ACOS for R&D approval is received, the UIC OPRS does not release approved VA consent and recruitment documents until after the VA Liaison receives the written ACOS for R&D approval. In the instances of VA Central IRB submissions, the investigator receives the written ACOS for R&D approval directly from the Medical Administration Specialist, only then may the research be implemented.

The JBVAMC does not allow JBVAMC officials to approve research that has not been approved by either the Collaborative IRB or the VA Central IRB. Submissions are not forwarded to the ACOS for R&D and/or the R&D Committee for review until after the required approvals, as described above, are received. Therefore, if the IRB approval has not been obtained, a submission will not be forwarded for review by JBVAMC officials.

VI. Affiliate and Central IRB Undue Influence

The Collaborative IRB and the VA Central IRB function as independent authorities to carry out the responsibilities required of an IRB. Any attempt to unduly influence members of the IRB and/or the IRB staff threatens the independence of the IRB and must be reported.

Allegations of undue influence for research reviewed by the Collaborative IRB should be reported as described in the UIC policies *Undue Influence of IRB Members and OPRS Staff* and *Executive Committee Supporting the Collaborative IRB*.

Reporting Procedures for the Collaborative IRB

- A. Collaborative IRB members should report this behavior to a Co-Chair of the IRB.
- B. Collaborative IRB Co-Chairs should report this behavior to the Director of OPRS, the UIC IO, and the JBVAMC Medical Center Director.
- C. UIC OPRS Staff should report this behavior to the Director of OPRS.
- D. If a Collaborative IRB member, including a Co-Chair, or OPRS staff believe that the undue influence is coming from either an IRB Co-Chair or Director of OPRS, they should report the allegation directly to the UIC IO and the JBVAMC Medical Center Director.

Investigative Procedures for the Collaborative IRB

- A. If the allegation appears to have merit, the Executive Committee (EC) serves as the investigative committee.

- B. The JBVAMC or NU representatives of the EC are responsible for investigating complaints of undue influence originating from their respective sites.
- C. The JBVAMC and NU are responsible as delineated in their respective MOUs for their institutional role in undue influence investigations.
- D. Any member of the EC having a conflict of interest with the allegation of undue influence is expected to identify the existence of a conflict and recuse themselves from the committee's discussion of the matter.

Allegations of undue influence for research reviewed by the VA Central IRB should be reported as described in the VA Central IRB policy *VA Central Institutional Review Board (IRB) Authority, Responsibilities, and Activities*.

VII. Human Subjects Determination

The JBVAMC relies on the Collaborative IRB and the VA Central IRB to make the determination of whether or not the proposed research activity represents human subjects research. The Collaborative IRB generally applies the DHHS definition for research involving human subjects, except when the activity is FDA-regulated the FDA definition is applied. JBVAMC investigators, staff, and students who intend to conduct activities that may in part represent research with human subjects as outlined in VHA Handbook 1200.05 and the UIC policy and procedure, *Institutional Authorization for Determining whether Research or Other Activities Represent Human Subjects Research*, are not authorized to determine independently whether the project is subject to the HSPP, except in limited circumstances.

If the determination is to be made by the Collaborative IRB, JBVAMC investigators, staff, and students must complete and submit the form, [Determination of Whether an Activity Represents Human Subjects Research](#), to the Collaborative IRB for all activities that involve human subjects and might represent human subjects research. After the R&D Office reviews the IRB and R&D applications for completeness, the investigator may submit the completed form to the Collaborative IRB office at UIC. An Assistant Director will communicate the decision promptly via email and/or letter communication to the investigator and JBVAMC R&D Office. The ACOS for R&D reviews the IRB determination and notifies the investigator of the determination and approval to initiate the research at the JBVAMC. When the human subject research determination is made by the VA Central IRB, the procedures and forms provided at their website are followed.

Four specific activities that the JBVAMC HSPP through the Collaborative IRB and UIC OPRS has determined do not represent human subjects research and do not require submission for a human subjects research determination are:

- A. Access to specified public use datasets (please refer to UIC Policy and Procedure, *Institutional Authorization for Determining whether Research or Other Activities Represent Human Subjects Research*, for a list of applicable data sets);
- B. Course-related activities designated specifically for educational or teaching purposes, where data is collected from and about human subjects as part of a class exercise or assignment but are not intended for use outside of the classroom (not intended to develop or contribute to generalizable knowledge);
- C. Case reports involving the observation of a single patient whose novel condition or response to treatment was guided by the care provider's judgment regarding the best interest of the individual; and

- D. Research which is limited to death records, autopsy records, or cadaver specimens provided that the cadaveric tissues/cells are not used for clinical investigations.

The individuals within the OPRS who can provide a determination about whether an activity at JBVAMC constitutes research involving human subjects is the Collaborative IRB Chair or designee, the UIC OPRS Assistant Directors or coordinators designated by the OPRS Director in consult with the Collaborative IRB Chair as being qualified to make this determination, and the UIC OPRS Associate Director and Director.

All individuals who make the determinations use the Determination of Whether an Activity Represents Human Subjects Research pre-review and review guide when making their determination. An Assistant Director communicates the decision promptly via email and/or letter communication to the investigator and JBVAMC R&D Office.

When the VA Central IRB determines that a given project does not constitute research, or does not constitute human research, it will provide a written letter with its decision to the PI who is responsible for providing the letter to the JBVAMC R&D Office.

VIII. Exempt Research

Definition: Exempt research includes research activities in which the only involvement of human subjects is in one or more of the categories listed in 38 CFR 16.101(b). The exempt status must be determined by the Institutional Review Board (IRB) Chair or an IRB voting member designated by the Chair. NOTE: Such an exemption applies only to requirements found in 38 CFR Part 16. All other relevant VA and Federal requirements apply.

Research in which activities involving human subjects are limited to one or more of the categories at 45 CFR 46.101(b) [38 CFR 16.102(b)] may qualify for exemption from 45 CFR 46 and 38 CFR 16. The Common Rule exemptions at 38 CFR 16.101(b) may not be applied to FDA-regulated research (see 21 CFR 56.104 for exemptions applied to FDA-regulated research). JBVAMC investigators, staff, and students do not have the authority under federal guidance, VHA handbook 1200.05 and the JBVAMC HSPP policy to independently determine that research involving human subjects is exempt. Investigators must submit the research to Collaborative IRB or the VA Central IRB for review of a claim of exemption and receive written documentation of the determination from the ACOS for R&D if reviewed by the Collaborative IRB or directly from the VA Central IRB if they review the research.

For investigators using the Collaborative IRB, the UIC OPRS Claim of Exemption application and policy, Exempt Review of Research, provide guidance to researchers on preparing and submitting a claim of exemption. For the IRBs, the UIC OPRS policy, Exempt Review of Research, and exempt review guide assists with their review of exempt research.

When the exempt determination is made by the VA Central IRB, the procedures and forms provided at their website are followed.

Collaborative IRB: After the R&D Office reviews the IRB and R&D applications for completeness, the investigator submits an original and one copy of the following documents to OPRS:

1. Claim of Exemption Application: This form is available on the OPRS website. The website also provides instructions for preparing the form and a list of documents to be submitted with the application;
2. Protocol;
3. Federal grant or grant subcontract (if applicable);

4. Appendices and supplemental documents as needed (e.g., Appendix P, Appendix K, questionnaires, surveys, letters of agreement, limited data use agreements, etc.);
5. Informed consent and recruitment materials, as appropriate.

The OPRS office/data entry staff checks the submission for completeness, documents receipt of the application, logs the application into the database, and assigns the protocol to the appropriate reviewer. For JBVAMC research, the following individuals may review and approve claims of exemption: IRB chair or IRB members designated by the Chair. The reviewer is responsible for notifying the IRB Chair or OPRS Director if they have a conflict of interest as outlined in the UIC HSPP policy [IRB Member, Ad Hoc Consultant, and OPRS Staff Conflict of Interest](#) or if they do not feel qualified to review the proposal. The reviewer uses the UIC OPRS [Claim of Exemption Guide for Reviewers](#) form to guide and document the review.

In making the determination, the reviewer considers whether:

1. The research meets the definition of research involving human subjects;
2. The selection of subjects is equitable;
3. The research involves no more than minimal risk;
4. The research involves prisoners;
5. The research involves children;
6. The research activities fit one or more exemption categories;
7. The research is FDA regulated;
8. The proposed recruitment procedures and consent process are appropriate;
9. The consent process, when applicable, informs participants of the following:
 - a) The activity is research;
 - b) Name, affiliation, and contact information for the investigator
 - c) Purpose of the research;
 - d) Description of the procedure;
 - e) Participation is voluntary;
 - f) Measures to protect the privacy of subjects and the confidentiality of the research data;
 - g) Description of any reasonable foreseeable risks as well as anticipated benefits;
 - h) Statement that the researcher is available to answer any questions.
10. Adequate provisions exist, when applicable, to protect privacy interests of subjects and maintain the confidentiality of the data.

The reviewer makes one of the following determinations:

1. Certification of exemption is granted;
2. Additional information or modifications needed before a final determination can be made;
3. Proposed activity does not meet the definition of research involving human subjects;
4. Research proposal does not meet the criteria for exemption and must be reviewed by the IRB under expedited or convened review processes;
5. For research meeting the criteria for exemption category 4 and involving the retrospective review of medical records, the reviewer determines whether a waiver of HIPAA authorization is warranted.

Collaborative IRB Communications. The investigator is promptly notified of the reviewer's determination by e-mail and campus or U.S. mail. The IRB is notified of protocols granted an exemption by listing them on the agenda for the next IRB meeting. The meeting minutes related

to the agenda also list the protocols granted an exemption during that time period. The OPRS notifies the JBVAMC R&D committee of the exemption determination by transmitting a copy of the determination letter and IRB minutes to the R&D office. The ACOS for R&D reviews the IRB determination and notifies the investigator of the determination and approval to initiate the research at the JBVAMC. After the JBVAMC R&D ACOS has reviewed and approved the research, any consent and recruitment documents are released to the PI by the UIC OPRS.

Although continuing review by the Collaborative IRB is not required, Investigators conducting exempt protocols at the JBVAMC must also submit an annual report of research activities directly to the JBVAMC R&D committee.

Studies granted exemptions from IRB review are issued an expiration date of three years. Investigators are sent reminders at 90, 60, and 30 days before the expiration date. Investigators must either re-submit to continue the research or submit a final report to close the protocol.

VA Central IRB. If VA Central IRB determines that a given project is exempt from IRB review, it will provide a written letter with its decision to the PI who will then be responsible for providing the letter to all Local Site investigators to share with their respective participating local VA facilities.

IX. Investigational Drugs and Devices

Investigators must provide in the materials they submit to the Collaborative IRB or to the VA Central IRB sufficient information for the respective IRB to make an approval determination and to ensure compliance with all VA, FDA, and other requirements.

For more information regarding the specific processes of the JBVAMC Pharmacy, refer to the *SOP Procedures for the Handling of Investigational and Clinical Trial Drugs*. For more information regarding the specifics of the Collaborative IRB, please refer to the UIC policy *Research Involving the Use of Drugs, Biologics, or Medical Devices*.

X. MULTI-SITE STUDIES

If conducting human research studies involving more than one engaged institution, each institution is responsible for safeguarding the rights and welfare of human subjects entered at its site, and for complying with all applicable local, VA, and other Federal requirements.

Multi-site trials are covered under this definition if any of the following apply:

- (1) VA is a sponsor;
- (2) VA functions as the coordinating center;
- (3) VA subcontracts to a foreign site;
- (4) The PI for the total study is a VA investigator; or
- (5) The VA investigator is specifically collaborating with an international investigator and the VA investigator sends data or human biological specimens outside the U.S., or receives them from outside the U.S.

NOTE: *This requirement does not apply if VA is only one of the participating sites and the trial does not meet the preceding conditions (e.g., pharmaceutical studies).*

XI. International Research.

Permission must be obtained from the CRADO, or designee, prior to initiating any VA-approved international research. This applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including agreements, MOU, Cooperative

Research and Development Agreements (CRADA), grants, or contracts. The CRADO, or designee, will not grant permission for an international research study involving prisoners as research subjects.

FWA and Approval. All international sites must hold an international FWA, and the research must be approved by the IRB or Research Ethics Board of the participating site(s) that are listed on the international FWA.

VA Medical Center Director's Responsibilities for international research include: (1) Approving the request for permission to conduct international research prior to forwarding it to the CRADO for action. (2) Ensuring permission has been obtained from the CRADO, or designee, for the international research prior to its initiation by an investigator at the facility. *Information on how to request permission may be referenced on the following Web site at:*

<http://www.research.va.gov/resources/policies/docs/instructions-intl-research.pdf>

Research Conduct. All international research must be conducted in accordance with VA requirements and all other applicable federal requirements for protecting human subjects, tissue banking, use of databases, federal criminal laws, and the standards of ethical conduct for employees of the executive branch.

XII. Investigator Responsibilities.

Refer to JBVAMC Investigator Manual for more detailed information.

XIII. Organizational Structure of the HSPP.

A. The JBVAMC HSPP is an integrated system that has organization-wide and agency support and encompasses all aspects of human subjects research enterprise, spanning the continuum of research design to study closure.

B. Roles and Responsibilities of the Components of the JBVAMC HSPP:

1. **JBVAMC Institutional Official (IO):** The JBVAMC institutional authority for the HSPP rests with the Medical Center Director who by example and mandate sets the tone that supports the primacy of human subjects protections through the review, draft, or recommend revision of JBVAMC R&D policies and procedures, policies and procedures related to the Collaborative IRB, and educational opportunities for R&D and IRB members, relevant administrative staff, and all members of the research team.

Adequate Resources. The Medical Center Director is responsible for ensuring the provision of adequate resources to support the operations of the HSPP, including but not limited to administrative resources including space and personnel, so that the program is in compliance with all VA and other federal requirements that govern human subjects research protection.

Knowledgeable Staff. The Medical Center Director is responsible for ensuring that IRB members, relevant administrative staff, and all members of the VA research team are appropriately knowledgeable to fulfill their respective duties in accordance with ethical standards and all applicable local, VA and other Federal requirements.

Human Research Protection Training. The Medical Center Director is responsible for ensuring that VA human subjects protection training requirements are met.

Local VA Facility's Responsibilities When Using the Collaborative IRB as an IRB of Record. The Medical Center Director, when using the Collaborative IRB as an IRB of Record, is responsible for:

- 1. Signing the MOU. The Medical Center Director** is responsible for signing the MOU with the University of Illinois at Chicago, the organization providing the IRB.
- 2. Ensuring Compliance by the Collaborative IRB, the External IRB.** The Medical Center Director is responsible for ensuring the Collaborative IRB, which is the external IRB of record, complies with all applicable VA and other Federal requirements including, but not limited to, the provisions of VHA Handbook 1200.05 when reviewing VA research. If the terms of the MOU are not met, the VA facility must make alternative IRB arrangements.
- 3. Appointing VA Representatives to the External IRB.** The Medical Center Director is responsible for appointing two or more VA-compensated employees who hold a minimum of 5/8th VA-compensated appointments as representatives to serve as voting members of the Collaborative IRB, unless a waiver for such representation is obtained from the CRADO.
 - a. These representatives may not include WOCs from the VA facility, or those with IPA appointments.
 - b. At least one of these representatives must have scientific expertise.
 - c. The representatives must serve as full-voting members of the Collaborative IRB; when relevant, this includes reviewing non-VA research matters coming before the IRB.
 - d. At least one of the representatives must be present during the review of the JBVAMC's research at a convened IRB meeting.

NOTE: As UIC has more than one IRB, this provision applies only to the Collaborative IRB, which is the IRB designated to review VA research.

Local VA Facility's Responsibilities When Using the VA Central IRB as an IRB of Record. The Medical Center Director, when using the VA Central IRB as an IRB of Record, is responsible for:

1. Retaining ultimate responsibility for oversight of the local HSPP including:
 - a. Ensuring that all research approved or determined exempt by the VA Central IRB is submitted to the local site R&D Committee for review.
 - b. Safeguarding the rights and welfare of human subjects of all research approved by the R&D Committee.
 - c. Educating the members of the research community to establish and maintain a culture of compliance with all VA and other Federal requirements, as well as JBVAMC requirements relevant to the protection of human subjects.
 - d. Instituting appropriate local oversight mechanisms to ensure compliance with the determinations of VA Central IRB. This includes performing routine audits and monitoring of locally conducted VA Central IRB-approved projects and reporting results of these activities to VA Central IRB.
 - e. Promptly informing VA Central IRB of any complaints from subjects or others; unanticipated problems involving risks to subjects or others; serious adverse events that are unanticipated and relate to the research; suspension or termination of research activities; or serious or continuing noncompliance encountered in VA human subjects research projects approved by VA Central IRB. The JBVAMC will work with VA Central IRB to ensure all VA and other Federal reporting requirements are met included, but not limited to, those specified in VHA Handbook 1058.01, Research Compliance Reporting Requirements.
2. Modifying the existing FWA, through ORO per VHA Handbook 1058.03, to designate VA Central IRB as an IRB of record. In addition, as the JBVAMC uses a local academic affiliate's IRB as an IRB of record, the JBVAMC will review the MOU it holds with the UIC,

and, if necessary, modify the MOU between the JBVAMC and UIC to permit the JBVAMC to use the VA Central IRB.

3. Maintaining documentation that all required training, credentialing and privileging is up to date for all local HSPP staff and for all local research team members of VA Central IRB-approved projects.
4. Working with LSI in preparing the Local Site Application to participate in any research project that has been designated for review by VA Central IRB. The LSI will submit the Local Site Application to the PI and VA Central IRB through the JBVAMC ACOS for R&D.
5. Providing comments and/or suggestions to VA Central IRB about VA Central IRB's initial review considerations in a timely manner, not to exceed 30 calendar days, from the date of receipt of the initial review considerations.
6. Notify the LSI and VA Central IRB in a timely manner, not to exceed 10 calendar days after receipt of VA Central IRB's final approval of a project, whether or not the local site chooses to participate or declines to participate in the project.
7. Ensuring the project is reviewed at the next regularly scheduled meeting of its R&D Committee after it agrees to participate in a given VA Central IRB-approved project.
8. Ensuring that the project is not started until it has been approved by *both* VA Central IRB and the local R&D Committee.
9. Forwarding any Freedom of Information Act (FOIA) requests received by JBVAMC for any records concerning VA Central IRB documents to the VHA Central Office FOIA Officer for review and release as applicable.
10. Agreeing not to independently modify any VA Central IRB-approved protocol except where necessary to eliminate apparent immediate hazards to the human subjects in accordance with 21 CFR 56.108(a) and 38 CFR 16.103(b)(4).
 - a. VA Central IRB must be notified within 5 working days if such an action is taken.
 - b. VA Central IRB will not review emergency use of test articles. Such use must be reviewed at the local level in accordance with the JBVAMC policies and procedures.
11. Notifying VA Central IRB immediately of potential research impropriety, misconduct, suspension, debarment, or restriction of any local research team member associated with a VA Central IRB-approved project.
12. Providing VA Central IRB access to the research subjects' clinical records and/or case files if required as part of any VA Central IRB oversight or monitoring activity. This includes providing access to any VA Central IRB member, administrative staff, or designee.
13. Participating in the annual review of the VHA Central Office HRPP, including an evaluating of VA Central IRB composition and operations, in accordance with VA Central IRB SOPs and as required by VHA Handbook 1200.01, the R&D Committee Handbook.
14. Maintaining compliance with any additional state, local, or institutional requirements related to the protection of human subjects. JBVAMC should consult its VA Regional Counsel Office or Office of General Counsel as needed.
15. Promptly notifying VA Central IRB and the PI of any changes in the local study team on active projects.
16. Providing procedures for coordinating approval of local committees, including but not limited to the R&D Committee, Radiation Safety Committee, Biosafety Committee, Institutional Animal Care and Use Committee (IACUC), and/or any other relevant local committees in accordance with local SOPs. Copies of such approval must be submitted to VA Central IRB.
17. Conducting routine compliance audits and monitoring and report findings to appropriate regulatory authorities and VA Central IRB. This includes any audits or monitoring plan included in VA Central IRB final approval of the project.

18. Maintaining a file on each VA Central IRB-approved project that will include the PI's Initial Application, the JBVAMC's Local Site Application, VA Central IRB-approved consent form that will be used locally, other documents associated with the initial application; VA Central IRB final approval documents, JBVAMC R&D Committee approvals, local audits and monitoring reports, and any subsequent correspondence, amendments, continuing review reports and approvals, and any other pertinent documents.
19. Providing information as requested to the JBVAMC LSI and the project's PI as part of the continuing review process.
20. Maintaining current written SOPs that incorporate JBVAMC's specific responsibilities as outlined in the MOU.
21. Complying with all VA Central IRB SOPs as applicable.
22. The JBVAMC will not:
 - a. Submit a Local Site Application for a specific project to VA Central IRB if another IRB of record for JBVAMC has already disapproved that VA facility's participating in the project.
 - b. Submit an application to another IRB of record for review if VA Central IRB has determined that the JBVAMC should not participate in a specific project.
23. Upon approval of the MOU by both parties and the addition of the VA Central IRB as an IRB of record on the JBVAMC's FWA, the JBVAMC'S IO will provide a letter to VA Central IRB designating in writing which local official (e.g., ACOS for R&D, AO for R&D, R&D Committee Chair, local IRB Chair) is authorized to perform each of the following three functions on behalf of the JBVAMC (*Note: One local official may have the authority to perform all three functions, or each of the functions may be delegated to different local officials.*). The appointment letter must also include the names and contact information for each designated local official, including what function each official is performing if more than one is appointed.
 - a. Providing comments and/or suggestions to VA Central IRB in response to VA Central IRB initial review considerations.
 - b. Responding to VA Central IRB's final approval of the project on behalf of JBVAMC as to whether JBVAMC chooses to participate or declines to participate in the project.
 - c. Serving as the liaison among VA Central IRB, the LSI, and the JBVAMC for oversight, compliance, and monitoring purposes.

Correspondence. The Medical Center Director is responsible for being the point of contact for correspondence addressing human subjects research with OHRP, FDA, and VHA Central Office.

HSP Accreditation. The Medical Center Director is responsible for ensuring the VA facility's HSP is accredited by an organization approved by ORD to perform this function.

Credentialing and Privileging. The Medical Center Director is responsible for certifying that all personnel involved in research including, but not limited to, research office staff, investigators, and other research team members have appropriate credentials and privileges (when applicable) to perform their human research-related duties. For more information refer to the *SOP: Credentialing of Individuals Involved in Human Subjects Research at the Jesse Brown VA Medical Center.*

Research Subject Outreach Program. The Medical Center Director is responsible for ensuring a local Research Subject Outreach Program is implemented to include:

(1) **Communication About the Study.** A reliable mechanism must be provided for research subjects to communicate with research study investigators and with an informed VA representative who is independent of the research study in question. This is accomplished by providing contact information in the consent document.

(2) **Information About Volunteering in Research.** Investigators must make every reasonable effort to provide the informational brochure, “Volunteering in Research – Here Are Some Things You Need To Know,” (<http://www.research.va.gov/programs/pride/veterans/tri-fold.pdf>) to potential research subjects in settings where subjects may be recruited (e.g., clinic waiting areas), and to each prospective subject when that individual is approached to take part in a study.

(3) **Venues for Information and Input.** Venues must be provided for research subjects and their designated representatives to obtain information, discuss their questions and concerns, and offer their input.

(4) **Educational Activities.** When appropriate, educational activities must be made available for research subjects and their communities.

Advertising. The Medical Center Director is responsible for ensuring that recruiting documents, flyers, and advertisements for non-VA research are not posted within or on the premises of a VA facility. Posting of such documents may give the Veteran or visitors to the VA facility the impression that the non-VA study is VA-approved research, the VA supports or endorses the research, or that VA will pay for the research expenses that are incurred. General guidance may be posted within VA indicating that Veterans may speak with their health care providers if they wish to participate in research and that information on clinical trials is available at: www.clinicaltrials.gov.

Audits. The facility Director is responsible for ensuring appropriate auditing of local human subjects research studies to assess compliance with all applicable local, VA, and other Federal requirements including, but not limited to, ORO requirements. Refer to the **Research Compliance Officer Auditing SOP** for more information regarding the audit processes and procedures.

2. **JBVAMC Human Protections Administrator/ ACOS:** The JBVAMC ACOS for R&D has been identified by the IO as the point of contact with OHRP for human subjects protection issues, including the investigation and reporting of non-compliance matters. This individual plays a key role in ensuring that the institution fulfills its responsibilities under its FWA.

3. **Chief Of Staff.** The Chief of Staff has overall responsibility for all clinical and academic activities including research. The Collaborative IRB chair will directly consult with the JBVAMC COS for issues relating to lapses in IRB approval of protocols to determine whether the PI is allowed to continue follow-up with enrolled subjects and stop enrolling new subjects in that study protocol.

4. **Associate Chief of Staff (ACOS) for Research and Development.** The ACOS/R&D is responsible for the operation of the research program, providing administrative support to, and implementing the decisions of, the R&D Committee and the Collaborative IRB. He/she ensures that the administrative structure is in place and functioning effectively. The ACOS/R&D provides advice and assistance to the R&D Committee and the Collaborative IRB on administrative and

regulatory matters. The ACOS/R&D also provides advice and assistance to investigators on both scientific and administrative matters pertaining to VA research, including the requirements for conducting research involving human subjects. He/she serves as an *ex officio* nonvoting member of the R&D committee, and is assisted by the Research Office Staff including the Administrative Officer for R&D (AO/R&D) and the Human Subject Research Specialist.

5. Administrative Officer for Research and Development. The AO/R&D assists the ACOS/R&D in carrying out his/her responsibilities. The AO/R&D is responsible for the day-to-day operations of the Research Office. This includes supervising the staff that provide liaison with the Collaborative IRB, NU -IRB support for the VA R&D Committee, and fulfillment of HSPP training, security, and research privacy requirements. The AO/R&D works closely with the Research Compliance Officer to convey HSPP information to research staff and ensure that they meet compliance requirements. He/she is a member of the HSPP, and is an advising, non-voting member of the R&D Committee.

5a. R&D Office Staff. The R&D Office Staff verify completion of the JBVAMC R&D IRB Protocol Submission checklist and maintain a database of educational status. The R&D administration also manage telephone calls from investigators concerning general questions, comments, inquiries into educational status, proof of educational status inquiries, among other responsibilities.

6. Research Compliance Officer. The Research Compliance Officer is organizationally part of the Office of the Medical Center Director and is appointed by the Medical Center Director. The Research Compliance Officer (RCO) is responsible for the management of compliance activities related to human subjects research at the JBVAMC.

7. UIC Human Protections Administrator. The UIC faculty member or academic staff identified by the IO as the point of contact with OHRP for human subjects protection issues, including the investigation and reporting of non-compliance matters, and plays a key role in ensuring that the institution fulfills its responsibilities under its FWA.

8. UIC Assistant Director of Quality Improvement/ Quality Assurance: This individual works closely as a consultant to the JBVAMC R&D Office and RCO for regulatory matters, policies and procedures, provides education on an as needed basis, and evaluates the UIC HSPP. This individual also assists the JBVAMC in preparing for government audits, creating and implementing corrective action plans, and drafting response letters to the government. In addition, this individual is responsible (and reimbursed) for the JBVAMC AAHRPP accreditation, including annual report applications, hosting site visits, and leading the reaccreditation process.

Members of the R&D Office conduct routine audits of medical record flagging and the informed consent documents and the RCO, the ISO, and the Privacy Officer conduct both required and routine audits of the research protocols conducted at the JBVAMC. In addition, the IRB may request that the RCO, ISO, and/or Privacy Officer conduct protocol specific audits.

9. UIC Institutional Review Board 4 (Collaborative IRB): The Collaborative IRB is dedicated to VA Research and responsible for considering the criteria for approval delineated in the appropriate review guides and policies and procedures in including but not limited to DHHS, FDA, and VA) when reviewing all submissions (initial review, continuing review, amendments, modifications, unanticipated events). For more information, refer to the *Operating and*

Coordinating Procedures for the Administration of the Collaborative JBVAMC/NU/UIC IRB (UIC IRB #4).

10. **UIC Collaborative IRB Staff.** These individuals record all meeting minutes, copy comments made by IRB reviewers from review guides onto template letters to communicate results to investigators, and, as time permits, conduct pre-reviews of submissions to verify that all required documents are present. The responsibilities include, but are not limited to, providing status and operational updates on submissions, and managing the IRB member packet delivery process.

11. **UIC VA Liaison.** This individual communicates on a regular basis with the R&D Office administrative team about day to day operational matters and is responsible for filing the ACOS approval letters received from the R&D Office staff.

12. **VA Central IRB:** The JBVAMC also lists the VA Central IRB on its FWA form and this IRB is another option for VA Research. The JBVAMC does not permit review of research by any commercial IRBs. Refer to the *SOP: Use of the VA Central IRB* for more information.

13. **Collaborative IRB Executive Committee:** The EC has been organized to coordinate communication regarding human subjects protection among the Collaborative IRB Co-Chairs and the JBVAMC, UIC and NU staff and administration in accordance with the executed MOUs. The EC also may make recommendations regarding Collaborative IRB resources and review, draft, or recommend revision of UIC OVCR policies and procedures related to Collaborative IRB. The EC may assist the IRB in the review of allegations of non-compliance and the appropriate members of the EC coordinate compliance investigations with their respective institutions as necessary and as directed by the Collaborative IRB Chair and/or Collaborative IRB. Refer to the UIC policy *Executive Committee Supporting the Collaborative IRB* for more information

14. **Radiation Safety Officer/ Radiation Safety Committee (RSO/ RSC):** The Jesse Brown VAMC Radiation Safety Officer (RSO) is responsible for review of the Principal Investigator declaration form entitled "Human Research Protocol Radiation Dose Supplement" prior to submission of the protocol to the Collaborative UIC-IRB for review. The following review and approval process may not be bypassed. If the human research involves use of any ionizing radiation, whether radioactive material or x-ray, a dosimetry form must be submitted. The dosimetry form requires the Principal Investigator to declare whether the radiation procedures are clinically indicated (standard of care) or research related. Standard of care means that research subjects would receive the same type and number of radiation procedures if they did not participate in the research. If the radiation procedures are strictly standard of care, a radiation risk statement is not required to be included in the consent form; however, if the Principal Investigator elects to include a radiation risk statement, it must be accurate and appropriate. If any radiation procedure is research related (and not standard of care), accurate dosimetry information must be provided and the consent form must contain an accurate and appropriate risk statement. In either case, the RSO will review the Dosimetry Form and the consent form. In addition to the RSO review, all research related radiation procedures must be reviewed for approval by the Jesse Brown VAMC Radiation Safety Committee (RSC). If the dosimetry form indicates the radiation procedures are strictly standard of care, the RSO will complete a review within three working days of receipt and notify the R&D office of the results. If the dosimetry form indicates some or all of the radiation procedures are research related, the RSO will expedite the RSC review and will provide the R&D office with the results as soon as possible. The RSO and the RSC will not certify that the radiation procedures are standard of care or research related. Instead, the collaborative UIC-IRB is responsible for determining whether the Principal Investigator has properly categorized the types and numbers of radiation procedures correctly as clinically indicated (standard of care) or research related. The R&D Office will inform the

investigator that documents are ready to submit to the IRB. The investigator will drop off the UIC-IRB and R&D meeting packet to UIC-OPRS with the checklist signed by the Medical Administration Specialist for IRB review and approval.

The JBVAMC Radiation Safety Committee authorizes the use radiation-producing devices and radioactive material in clinical, education, research, and development activities. The RSO/ RSC establishes radiation policies and procedures for Jesse Brown VAMC in accordance with applicable regulatory requirements governing the procurement, use, storage, and disposal of radiation-producing devices and radioactive material.

15. JBVAMC Radioactive Drug Research Committee (RDRC): Based on previous recommendations of the FDA, the JBVAMC does not have a Radioactive Drug Research Committee at this time; however, the JBVAMC has agreed to form an RDRC if the need arises.

16. JBVAMC Laboratory Research and Environmental Safety R&D Subcommittee: This committee oversees investigators doing laboratory research and reports its findings to the R&D Committee.

17. JBVAMC Laboratory and Office Space Allocation and Equipment R&D Subcommittee: This committee oversees investigators office and laboratory space issues reports its findings to the R&D Committee.

18. Jesse Brown VAMC Research Audit Subcommittee: This committee conducts peer-to-peer audits to evaluate investigator compliance, such as auditing whether patients are appropriately flagged in CPRS.

19. JBVAMC Pharmacy: This unit is a component of the inpatient JBVAMC Medical Center. The pharmacy through the Investigational Drug Service is responsible for the handling and control of investigational drugs at JBVAMC. Refer to the SOP *Procedures for the Handling of Investigational and Clinical Trial Drugs* for more information

20. JBVAMC Research Integrity Officer. This individual focuses on integrity issues, such as data falsification.

21. UIC Center for Clinical and Translational Sciences. The CCTS offers services to investigators, such as protocol and informed consent development services. The CCTS also offers services to investigators such as nursing support, laboratory testing, bionutrition services, education, biostatistical support, informatics support, and administrative support. The CCTS review process provides an additional support mechanism for the IRB to address whether the research is using sound scientific design. Please look for additional information this summer about the status of the CCTS is in flux. The JBVAMC R&D Office meets with CCTS regulatory personnel quarterly.

22. NUCATS. The NUCATS is based at Northwestern University and offers services to investigators in the same manner as the UIC CCTS, including protocol and informed consent development services. The JBVAMC R&D Office meets with the NUCATS to orient the office to services.

23. JBVAMC R&D Committee: The JBVAMC R&D Committee reviews all research generally under the auspices of the JBVAMC, initially and at least once a year, including research determined exempt by the Collaborative IRB. All NU, UIC, or JBVAMC research that engages the JBVAMC as a recruitment or performance site must have the approval of the JBVAMC R&D

Committee and its appropriate subcommittees before the research may begin. The JBVAMC R&D Committee may not make regulatory determinations.

24. **JBVAMC Merit Review.** The JBVAMC R&D Office administers VA grants.

25. **West Side Institute of Science and Education.** This office handles all funding that does not directly arise from a VA source, such as the Department of Defense, the NIH, and non-federal sponsors.

26. **VA Central Office COACH:** This VA office provides informal regulatory assistance and interpretation to the JBVAMC R&D and UIC OPRS.

27. **VA Central Office Counsel:** This VA office provides JBVAMC R&D with language and required wording for applicable documents.

28. **VA Regional Counsel:** This VA office provides JBVAMC R&D and UIC OPRS with language and appropriate wording for applicable documents.

29. **VA Office of Research Oversight, Research Integrity and Assurance.** This VA office provides JBVAMC and affiliate OPRS with specialized expertise in providing current industry interpretation and enforcement of applicable VHA Handbooks.

30. **UIC Conflict of Interest Office:** For UIC and VA only investigators, this UIC office is responsible for identifying, reporting, and creating a management plan, if applicable, as to potential conflicts of interest that may affect human subject studies. The COI office provides information pertaining to the protocol specific conflict and makes a recommendation for management through the Statement of Explanation and Management (SEAM) form to the IRB for approval.

31. **JBVAMC HIPAA Privacy Officer:** Responsible for HIPAA privacy oversight for VA Research. The JBVAMC Privacy Officer attends the Collaborative IRB meetings to advise the IRB on privacy and functions as an advisor who does not vote with the IRB and is not an IRB member.

32. **JBVAMC Information Security Officer:** Responsible for Information Security for VA Research at the JBVAMC. The JBVAMC Information Security Officer attends the Collaborative IRB meetings to advise the IRB on information security issues as an advisor who does not vote with the IRB and is not an IRB member.

33. **JBVAMC Patient Rights Advocate:** Subjects in research involving the JBVAMC have access to this resource for any complaints. When patients are research subjects and the complaints involve a human subjects protection issue, this individual notifies the ACOS for R&D. A summary of the complaint and recommended resolution is forwarded to the JBVAMC R&D Committee with a copy to the Collaborative IRB.

34. **Education.** The JBVAMC relies on UIC OPRS to provide educational sessions concerning regulatory reminders and updates, AAHRPP requirements, and provides IRB and human subject protections related education to Collaborative IRB members, VA community members, VA investigators, VA research coordinator. Information is often disseminated through town hall meetings, the UIC OPRS newsletter emailed to a VA Research listserv of investigators. UIC OPRS maintains a list of formal educational sessions and VA Research topics presented. The VA Liaison and OPRS Director both provide regulatory guidance on an as-needed basis and day-to-day basis to the R&D Office as well as to the RCO and HPA concerning the content and

application of VHA Handbook information, JBVAMC SOPs, and UIC HSPP policies and procedures.

UIC OPRS IRB Assistant Directors and IRB Coordinators specially trained in VA Research are available for phone calls from investigators engaged in VA Research, as well as from the R&D Office or RCO, during OPRS office hours. The UIC OPRS IRB Assistant Director and IRB Coordinators also orient and provide regulatory guidance to the JBVAMC RCO through annual audits.

The R&D Office and RCO provide education on a day-to-day basis concerning educational requirements when taking phone calls from investigators, as well as providing relevant announcements at Town Hall meetings. The R&D Office also forwards emails sent regarding updates to VHA Handbooks or other VA requirements to UIC OPRS. The R&D Office sends updates to formulary information through a VA investigator listserve.

For more information regarding the specific requirements of the Collaborative IRB, please refer to the UIC policy *Investigator, Research Personnel, IRB Member and Staff Education Program and Training Requirements*.

35. Information Resources Management. This department provides technical support to the JBVAMC to ensure that the technical components are working properly to protect subject data and confidentiality.

XIV. Application of Laws

The VA has agreed to follow the Common Rule, incorporated in 38 CFR 16.

The procedures followed by the JBVAMC HSPP for implementing 38 CFR Part 16 are defined in VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research. These requirements also apply to VA research involving special populations such as pregnant women, children, and prisoners.

The JBVAMC HSPP adheres to the following:

38 USC 501, 7331, 7334 - Statutory provisions for protection of VA patient rights,
38 CFR 17.33a and 17.34 – VA regulations pertaining to VA patient rights
38 CFR 17.85 – VA regulations pertaining to research related injuries
38 CFR 17.45, 38 CFR 17.92 – VA regulations pertaining to hospital care for research purposes and outpatient care for research purposes
38 USC 5705 – VA confidentiality of medical quality assurance records statute
5 USC 552a, 38 USC 5701a and 7332, 45 CFR Parts 160-164 – Statutes and regulations pertaining to the release of patient information

VHA Requirements are provided in VHA Handbook 1605.1, Privacy and Release of Patient Information, and VHA Handbook 1605.2 – Minimum Necessary Standards for Protected Health Information

When FDA-regulated clinical investigations are conducted the JBVAMC HSPP applies the FDA regulations pertaining to the protection of the human subjects and the conduct of the IRBs, as does the Collaborative IRB and the VA Central IRB.

The following additional FDA regulations are also applied when research involves the use of specific test articles as follows:

- 21 CFR 312 and 314 – Investigational New Drug Applications
- 21 CFR 361 – Radioactive Drugs for Certain Research Uses
- 21 CFR 600 – Biological Products
- 21 CFR 812, 814 – Investigational Device Exemptions

VA Research supported by DHHS must also adhere to the provisions of 45 CFR 46.

VA Research must comply with the state and local laws of the appropriate jurisdiction of the VA facility where research is conducted.

For a complete list of applicable Illinois state laws, please refer to the UIC policy *Ethical Standards and Legal Principles*.

REVISION LOG:

| Version (#, date) | Replaces (#, date) | Summary of changes |
|--------------------------|---------------------------|---|
| 3.6, 11/25/09 | 3.6, 4/10/09 | |
| 3.8, 04/15/11 | 3.6, 11/25/09 | |
| 3.9, 07/13/11 | 3.8, 04/15/11 | Delegation of scientific validity review to IRB |