

LOUIS STOKES CLEVELAND  
VA MEDICAL CENTER  
10701 East Boulevard  
Cleveland, OH 44106

MEDICAL CENTER POLICY 151-018  
September 1, 2007

## HUMAN RESEARCH PROTECTION PROGRAM

1. **PURPOSE:** To establish policy and procedures as it relates to the Louis Stokes Cleveland Department of Veteran Affairs Medical Center (LSCDVAMC) Human Research Protection Program (HRPP). The purpose of this program is to foster a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the LSCDVAMC and to ensure compliance with all VA policies as well as all federal, state, and local laws and regulations.

### 2. **POLICY**

a. The LSCDVAMC has established a HRPP which oversees the review and conduct of research involving human subjects under the auspices of the LSCDVAMC.

b. The HRPP is a multi-tiered program involving the Medical Center Director, Chief(s) of Staff, Associate Medical Center Director, Associate Chief of Staff for Research and Development (ACOS/R), Administrative Officer for Research and Development, Research and Development Committee, Institutional Review Board (IRB), IRB Administrator and Staff, Subcommittee on Research Safety, Research Safety Coordinator/Chemical Hygiene Officer, Research Quality Improvement Program and the Research Oversight Committee, Conflict of Interest Committee, Research Compliance Officer (RCO), Conflict of Interest Administrator, Research Credentialing Coordinator, Research Service Program Analyst, Research Information Resource Manager, Executive Director, Staff, and Board of Trustees of the Cleveland VA Medical Research and Education Foundation, Investigators, Study Staff, Research Subjects/Participants, Medical Executive Committee, Pharmacy Service, Pharmacy & Therapeutics Committee, Environment of Care Committee, Radiation Safety Committee, Radiation Safety Officer, Information Security Officer, Risk Management and the Patient Advocates, Patient Care Administrative Staff, Privacy Officer, Regional Counsel's Office, Case Western Reserve University, Case IRB Advisory Committee, Case Conflict of Interest Advisory Committee, and the Case Institutional Biosafety Committee.

c. The HRPP includes mechanisms to:

- (1) Establish a formal process to monitor, evaluate, and continually improve the protection of human research participants.
- (2) Dedicate resources sufficient to do so.
- (3) Exercise oversight of research protection.
- (4) Educate investigators and study staff about their ethical responsibility to protect research participants.

- (5) When appropriate, intervene in research and respond directly to concerns of research participants.
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d. The HRPP will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (often referred to as the Belmont Report) and will be performed in accordance with the policy and regulations found in Department of Veteran Affairs VHA Handbook 1200.1, VHA Handbook 1200.5, 38 Code of Federal Regulations (CFR) 16, 45 CFR 46 and 21 CFR 50 and 56. The actions of LSCDVAMC will also conform to all other applicable federal, state, and local laws and regulations.

e. The LSCDVAMC will designate the Medical Center Director as the Institutional Official (IO) who has overall responsibility for the LSCDVAMC HRPP. The duties of the IO are as follows:

- (1) Be responsible for compliance with institutional policies and all applicable regulations for the protection of human subjects.
- (2) Be the signatory authority for the Federal-wide Assurance to the Office of Human Research Protections.
- (3) Provide support to the human research protections program within the means of the institution.

f. In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to fulfill these duties.

g. To conduct its responsibility effectively, the LSCDVAMC maintains an IRB to review research protocols involving human subjects. The IRB is an autonomous administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the LSCDVAMC. The IRB has the following authority to:

- (1) Approve, require modifications to secure approval, or disapprove human subject research activities overseen and conducted under the auspices of the LSCDVAMC.
- (2) Suspend or terminate research for continued noncompliance with the Common Rule, VA, Department of Health and Human Services (DHHS), and Food and Drug Administration (FDA) regulations, or its own findings, determinations, and requirements (38 CFR 16.113).
- (3) Suspend or terminate research that has been associated with unexpected serious harm to participants.

- (4) Observe and/or monitor LSCDVAMC research (including the consent process) to whatever extent it considers necessary to protect human subjects.
- (5) Review copies of reports, audit findings, or correspondence to or from any regulatory agency (such as the VA Office of Research Oversight (ORO), Office of Human Research Protections (OHRP), or the FDA) that bear upon the protection of human subjects in research in which they are involved.
- (6) Bring any matter directly to the attention of the LSCDVAMC IO, the ACOS/R, RCO, or Regional Counsel when warranted.

h. All IRB approved research studies are subject to ongoing review, which must be conducted at least once annually by the IRB. If approval by the IRB lapses, all research activity must stop unless the IRB finds that there is an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating in the research interventions or interactions.

i. The IRB has jurisdiction over all human subject research conducted under the auspices of the LSCDVAMC. Research considered under the auspices of the LSCDVAMC includes all research involving human subjects that is conducted completely or partially in LSCDVAMC facilities, conducted in approved off-site locations, facilities, and/or conducted by LSCDVAMC researchers, employees, or agents, while on official VA duty time. It includes research conducted using non-public patient data from VA records, using VA resources, publishing or presenting results with the VA cited as supporting or conducting the research, or recruiting VA patients at VA facilities. The research may be VA funded, funded from non-VA sources, or conducted without direct funding.

j. Investigators receiving support from other Federal agencies, such as the National Institutes of Health, must meet requirements for the protection of human subjects of the funding source in addition to those of VA. Where FDA-regulated test articles are used, the FDA regulations apply regardless of funding source (21 CFR Parts 11, 50, 54, 56, 312, 314, 600, 812, and 814).

k. All institutional and non-institutional performance sites for the LSCDVAMC, domestic or foreign, will be obligated by this policy to conform to ethical principles which are at least equivalent to those of the LSCDVAMC and will comply with VHA Handbook 1200.16, "Off-Site Research."

### **3. RESPONSIBILITIES**

a. The IO, R&D Committee, and the IRB shall adopt operating procedures to implement this policy. These procedures shall be reviewed and approved by the LSCDVAMC Research & Development Committee and will serve as the governing procedures for the conduct and review of all human research conducted under the auspices of the LSCDVAMC.

#### 4. DEFINITIONS

a. **Human Subject.** A human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through identifiable private information (38 CFR 16.102(f)). The definition provided in the Common Rule includes investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled. As required by 38 CFR 16.102(f) an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

For research covered by Food and Drug Administration (FDA) regulations (21 CFR 50 and 56), human subject means an individual who is or becomes a participant in a clinical investigation (as defined below), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In research involving devices, a human 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 (21 CFR 812).

b. **Research.** Research is defined as the testing of concepts by the scientific method or formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis and/or research question. The Common Rule (38 CFR 16) defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.

Under FDA regulations, the terms *research* and *clinical investigation* are deemed to be synonymous.

c. **Clinical investigation.** A clinical investigation is defined as any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the 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. The term does not include experiments that must meet the provisions of part 58, regarding non-clinical laboratory studies. An experiment, as defined in 21 CFR 312, includes any use of a drug other than the use of a marketed (approved) drug in the course of medical practice.

d. **Test Article.** A test article is a drug, device, or other article including a biological product used in clinical investigations involving human subjects or their specimens.

e. **IRB.** An IRB is a board established in accordance with and for the purposes expressed in the Common Rule (38 CFR 16.102(g)). The IRB is a subcommittee of the R&D Committee.

f. **Institutional Official (IO).** The IO is the medical center Director. The IO is the VA official responsible for ensuring that the HRPP at the facility has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research.

g. **Principal Investigator (PI).** A PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. FDA considers PI and investigator as being the same.

h. **Responsible Investigator (RI).** A RI is an investigator that assumes ultimate responsibility for the conduct of the research. A RI is named in the protocol if the PI (1) has a without compensation (WOC) appointment; (2) is a student, resident, or fellow; (3) is not credentialed to perform and/or supervise the study procedures; and/or (4) is not qualified to be responsible for study related healthcare decisions. A RI must have a paid VA appointment.

i. **Co-Investigator (Co-I).** A Co-I is an individual who, under the direction of the PI, is involved in some or all aspects of the research project, including the: design of the study, conduct of the study, analysis and interpretation of identifiable data, and writing of manuscripts resulting from the project.

j. **Research under the Auspices of the LSCDVAMC.** Research considered under the auspices of the LSCDVAMC includes all research involving human subjects that is conducted completely or partially in LSCDVAMC facilities, conducted in approved off-site locations, facilities, and/or conducted by LSCDVAMC researchers, employees, or agents, while on official VA duty time. It includes research conducted using non-public patient data from VA records, using VA resources, recruiting VA patients at VA facilities, publishing or presenting results with the VA cited as supporting or conducting the research, or recruiting VA patients at VA facilities. The research may be VA funded, funded from non-VA sources, or conducted without direct funding.

**4. REFERENCES:** 38 CFR Parts 16 and 17; 45 CFR 46, Subparts A-D; 21 CFR 50, 56, 312, 361 and 812; VHA Handbook 1200.1 "Research and Development Committee"; VHA Handbook 1200.5 "Requirements for the Protection of Human Subjects in Research"; Medical Center Policy 119-013 "Pharmacy and Therapeutics Committee"; Medical Center Policy OOIH-021 "Environment of Care Committee"; Medical Center Policy 000-027 "Radiation Safety Management Program"; Medical Center Policy 119-019 "Investigational Drugs for Patient Use"; Medical Center Policy 151-009 "Credentials and Training of Employees Involved in Human Subjects Research"; Human Research Protection Standard Operating Procedures; Medical Center Policy 151-001 "Research and Development Committee"; Medical Center Policy 151-002 "Establishing an Institutional Review Board"; Medical Center Policy 151-007 "Subcommittee on Research Safety"; Medical Center Policy 151-012 "Policies and Procedures for Conducting Research"; Medical Center Policy 151-016 "Noncompliance in Research"; IAC Policy and Procedures; Quality Improvement Program for Human Subjects Research SOP; Medical Center Policy 000-010 "Administrative Boards of

Investigations”; Medical Center Policy 000-008 “Patient Advocacy Program”; “Cooperative Studies Program: Guidelines for the Planning and Conduct of Cooperative Studies,” 2007; VHA Handbook 1200.17 “VA Research and Education Corporations”; VHA Directive 2003-031, “Establishment of a Facility Human Protections Program

**7. RESCISSION:** Medical Center Policy 151-018 dated September 1, 2004 was rescinded. The rescission date of this Policy is September 1, 2010.

**8. FOLLOW UP RESPONSIBILITIES:** Associate Chief of Staff for Research

WILLIAM D. MONTAGUE  
Medical Center Director

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