

CONDUCTING RESEARCH

1. **PURPOSE.** To establish policies and procedures for conducting research studies at the Louis Stokes Cleveland Department of Veterans Affairs Medical Center (LSCDVAMC), which use VA patients or VA resources, and involve VA employees, including part-time and full-time staff, as investigators or collaborators.

2. **POLICY.** To ensure that research conducted under or within the auspices of the LSCDVAMC be done so in accordance with all federal, local and VHA regulations.

3. DEFINITIONS

a. **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. For the purpose of this document, the term research includes clinical investigations as defined below.

b. 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.

c. **Research under the auspices of the LSCDVAMC.** Research considered under the auspices of the LSCDVAMC includes all research 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.

d. **Animal.** Any live vertebrate animal used or intended for use in research, research training, experimentation, or biological testing, or for a related purpose. An

animal for purposes of compliance with the Animal Welfare Act Regulations is any live or dead cat, dog, non-human primate, guinea pig, hamster, rabbit, or any other warm-blooded animal which is being used, or is intended for use in research, teaching, testing, or experimentation.

e. 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. (VHA Handbook 1200.5 "Requirements for the Protection of Human Subjects in Research")

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 above), 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).

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

g. VA Research is research that has been reviewed and approved by a VA Research and Development (R&D) Committee.

h. Institutional Official (IO). The IO is the medical center Director. The IO is the VA legally authorized signatory official for all institutional assurances with Office of Human Research Protections (OHRP), the Office of Laboratory Animal Welfare (OLAW), and the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). The IO ensures that research and its administrative functions, including the Human Research Protection Program (HRPP), the Animal Research Facility, the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), and the Subcommittee on Research Safety (SRS) at the LSCDVAMC has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects and animal research.

i. 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.

j. Responsible Investigator (RI). A RI is an investigator who 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.

k. 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.

4. RESPONSIBILITY:

a. **The Medical Center Director (Institutional Official)**, advised and assisted by the R&D Committee, is responsible for the R&D program at the medical center. The medical center Director delegates the authority to administer the R&D program to the Associate Chief of Staff for R&D (ACOS/R), who is responsible to the medical center Director through the Chief of Staff.

b. **The ACOS/R** is responsible for informing and instructing all eligible VA investigators about the policies and procedures for obtaining approval to conduct research.

c. **The R&D Committee** and its appropriate subcommittees must approve all research, regardless of funding source, which is conducted under the auspices of LSCDVAMC. No research project may commence prior to final and full approval by the R&D Committee. Full R&D Committee approval will not be granted until the appropriate subcommittees have granted full approval.

d. **The IRB** is responsible for review of all research involving human subjects that is conducted under the auspices of the LSCDVAMC.

e. **The IACUC** is responsible for reviewing all testing, research or training procedures involving the use of vertebrate animals conducted under the auspices of LSCDVAMC.

f. **The SRS** is responsible for coordinating all safety activities in the research laboratories and reviewing all research activities involving biological, chemical, physical and radiation hazard for compliance with all applicable regulations, polices and guidelines.

5. PROCEDURE:

a. To conduct research at the LSCDVAMC the PI must obtain approval of the R&D Committee and its subcommittees, as appropriate to the research, by submitting applicable documents to the Research Office (151W), Room K-115:

1) A completed Request to Review Research Proposal (RRRP) form including applicable referenced supplemental documents, e.g. budget, for all submissions.

2) If the proposed research involves human subjects, appropriate IRB forms must be prepared in accordance with the LSCDVAMC IRB requirements. * Documentation that the PI and all key personnel have completed both Human Subject Protection Education and Credentialing is required.

3) If the proposed research involves the use of experimental animals, the Animal Component of Research Protocol (ACORP) form must be prepared in accordance with VHA Handbook 1200.7. * Documentation that the PI and all personnel have received required training in protection of animals in research and completed credentialing is required.

4) A completed Research Protocol Safety Survey (VA Form 10-0398) prepared in accordance with VHA Handbook 1200.8. *

**Veterans Administration Central Office (VACO) has instituted a "Just in Time" policy of accepting proposals for VA funding without Subcommittee approvals with the stipulation that approval of these subcommittees and the R&D Committee must be received in VACO prior to distribution of funds.*

5) Documentation that the PI as well as study staff have completed VA Research Data Security and Privacy Training. This is an annual requirement.

6) The PI's curriculum vitae, including publications, if the investigator has not had a proposal approved within the previous five years.

7) Documentation that study staff (performing research duties at this facility) who do not have a VA paid appointment have received a VA WOC appointment.

8) Conflict of Interest Statements for all listed study staff.

9) Complete Data Security Checklist and Principal Investigator Certification for every research submission.

b. These documents should be assembled in the order listed on the RRRP form and the originals submitted to the Research Office (151W), K-115.

c. The R&D Committee meets monthly. All materials for R&D review must be received by published deadlines. The R&D Committee must evaluate scientific quality, the relevance to both VA's mission and the facility's research program, and the ability of the investigator to perform and complete the research. In addition, the review must include information on the use, storage, and security of VA data and VA sensitive information including VA Protected Information; the budget; the requirements for space, personnel, equipment and supplies; the role of the investigator at the facility; the investigator's qualifications and other information deemed relevant by the R&D Committee. If the project involves the use of veterans' data or another person's data (identified or de-identified), the review must include an assessment of the mechanisms in place to ensure: Security of data and all files; confidentiality of data, including data derived from research subjects; release of data in accordance with VHA regulations and policies and control of the data so that reuse of the data is within an approved research

protocol and in compliance with VHA procedures. The R&D committee must also assess potential conflict of interest.

d. The Cleveland VA Medical Research and Education Foundation (Foundation), the VA affiliated non-profit corporation established under PL 100-322 and 38 USC 7361-7368, is responsible for administering all non-VA funds from other non-federal government agencies, private proprietary companies, and voluntary agencies that VA staff use to conduct research. The medical center Director must approve any alternative administrative arrangements. The PI may request and provide a written justification for an exception to this policy at the time of submission of the research proposal to the Research Office. The R&D Committee will review the request and make a recommendation to the medical center Director. (VHA Handbook 1200.2 "Research Business Operations")

e. These procedures apply to all research projects whether funded or unfunded and regardless of funding source. If a research proposal is also to be submitted to VACO for review and funding, the proposal must be prepared in accordance with VHA Handbooks 1202.1 (Biomedical Laboratory and Clinical Science R&D), 1203.1 (Rehabilitation R&D), or 1204.1 (Health Services R&D) in addition to meeting these local requirements.

f. In submitting a research proposal for review, the PI will adhere to administrative and regulatory requirements of the research program including, but not limited to:

- 1) Overseeing the conduct of the study and supervising subordinate personnel;
- 2) Ensuring the study is conducted according to the highest ethical standards and integrity;
- 3) Protecting the rights and welfare of all participants in the study, including human subjects, laboratory animals, and research staff;
- 4) Maintaining strict adherence to guidelines protecting the identifiable information on human research subjects or their data;
- 5) Submitting required reports in a timely manner. This includes submitting continuing review applications at the intervals stipulated by the committees, applying for approval of any changes to a protocol prior to initiating them, reporting promptly any adverse events, submitting annual Data Security Checklist for Principal Investigators, and submitting a final report at study closure;
- 6) Providing financial reports for each proposal;
- 7) Providing bibliographic and biographic data;
- 8) Submitting manuscripts for review prior to publication;
- 9) Acknowledging VA support and affiliation on publications and presentations;

10) Disclosing any inventions or discoveries to the Department of Veterans Affairs;

11) Providing information requested regarding the conduct of the study; and

12) Complying with and assuring staff complies with applicable education requirements for conducting research.

6. **REFERENCES:** Medical Center Policy (MCP)151-001 "Research and Development Committee"; MCP 151-002 "Protection of Human Subjects in Research: Establishing an Institutional Review Board"; MCP 151-003 "Protection of Animal Subjects in Research: Establishing an Institutional Animal Care and Use Committee", MCP 151-007 "Subcommittee on Research Safety", MCP 151-014 "Research Service Financial Conflict of Interest ", VHA Handbooks 1200.1, 1200.2, 1200.4, 1200.5, 1200.7, 1200.8, and 1200.11; 38 USC 7361-7368;

7. **RESCISSION:** MCP 151-012 dated September 1, 2004 has been rescinded. The review date for this policy is September 1, 2010.

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

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Medical Center Director