

Human Research Protection Program

A. PURPOSE

The Nebraska-Western Iowa Health Care System (NWIHCS) is engaged in research involving human subjects. The Federal-wide Assurance (FWA) 00000556 has been approved for the NWIHCS. The institution becomes engaged in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes. Therefore, the Human Research Protections Program (HRPP) has been developed to ensure the rights, safety and welfare of all subjects recruited or enrolled in research projects, regardless of who conducts the research or the funding source. The purpose of this program is to monitor, evaluate and improve the protections of human research participants. The NWIHCS is also responsible for assuring that all personnel involved in research activities understand and comply with the ethical standards of research.

B. SCOPE

1. The HRPP is governed by and guided by the Belmont Report, the Federal Policy (Common Rule) codified by the Department of Veterans Affairs (DVA) at 38 CFR 16. In addition, the NWIHCS adheres to the Department of Health and Human Services (DHHS) regulations at 45 CFR 46, and the Food and Drug Administration (FDA) regulations at 21 CFR 50, 56, 312, 361, 812, and Veterans Health Administration (VHA) Handbook 1200.05. The types of activities that may be subject to IRB review and approval are clinical, behavioral and social sciences, epidemiological, patient record, repository, tissue banking, database, genetics research and quality assurance activities if they are designed or intended to contribute to generalizable knowledge. These are examples only and are not exhaustive of all human subjects research conducted within the NWIHCS. Clinical investigations involving a test article are also subject to the requirements of the FDA. The HRPP applies to all research involving human subjects that is conducted completely or partially in VA facilities, approved off-site locations or conducted by VA researchers while on official VA duty time. A Memorandum of Understanding Regarding Human Protections Oversight has been established between UNMC and the NWIHCS to clarify engagement, protocol review and reporting for investigators with dual appointments.

2. The ethical conduct of research requires the cooperation, collaboration, and trust among the institution, investigators, research coordinators, research team members, the participants who enroll in the research, sponsors, the IRB, the Research and Development Committee (R&D), other committees or subcommittees addressing human subjects protection (Biosafety, Radiation Safety, Conflict of Interest, etc.), Research Administrative Office (RAO) staff, and Pharmacy staff. The Research Compliance Officer (RCO) is responsible for auditing and reviewing research projects relative to

requirements for the protection of human subjects. All parties will share in the responsibility for the ethical conduct of research.

C. PROCEDURES

1. All IRB and R&D Committee members, HRPP staff, investigators and research team members who are involved in conducting human research are required to meet the requirements of the NWHCS Human Subjects Protection Program education and credentialing requirements. Continuing education is also mandated every two years.

2. Systematic budgeting for HRPP: Research Service will be responsible for reviewing regulatory requirements and changes regarding the HRPP program on an annual basis. Research service will prepare a budget/resource document that will itemize in detail projected resource requirements for the HRPP, for the upcoming fiscal year. This budget will be prepared to coincide with other budget activities of the Nebraska-Western Iowa Health Care System. The proposal will be submitted to the R&D Committee and reported to the Chief of Staff and the Medical Center Director through the R&D Committee meeting and minutes. Elements of this resource budget will include:

- a. Detail of personnel cost and areas of responsibility required for HRPP activities
- b. Supplies/Materials required
- c. Review of appropriate space needs in the context of maintaining external HRPP certification
- d. Equipment requirement and needs
- e. Training and education of individuals involved in the HRPP program

3. The not-for-profit corporation, Nebraska Educational Biomedical Research Association (NEBRA), also contributes support to the HRPP.

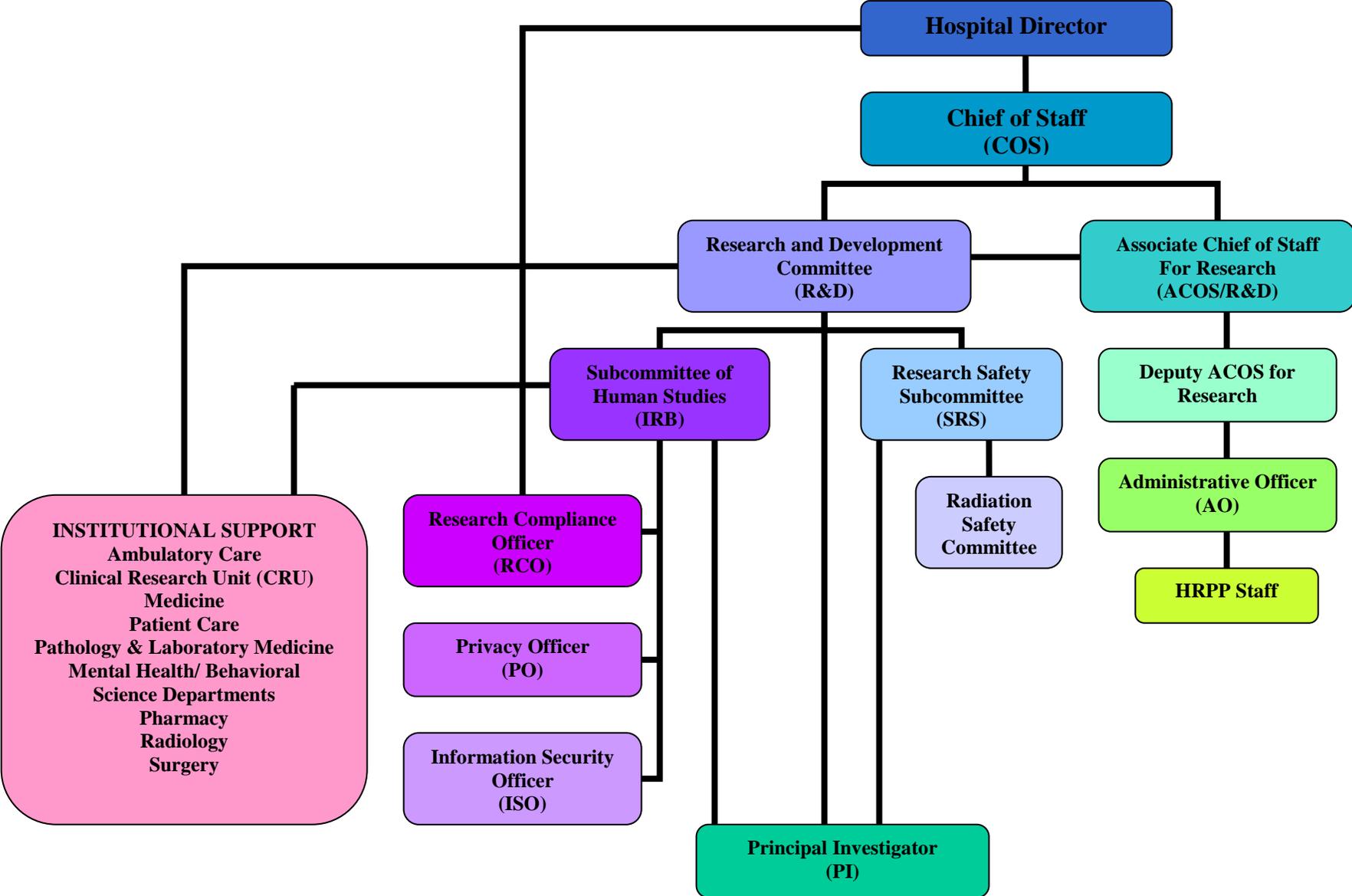
4. Sponsors share in the responsibility of following ethical standards and practices. The agreement among the Principal Investigator (PI), institution and sponsor in the form of a CRADA or contract is negotiated and reviewed for appropriateness and completeness by the Regional Counsel facilitated by NEBRA.

5. All requests to conduct human research will first be submitted to the HRPP staff for initial screening and to begin the process for IRB and R&D Committee review. Research does not commence until final approval is granted by the IRB, R&D Committee, ACOS/R&D and other applicable committees who address human subject protection.

D. ORGANIZATION

The following chart displays the organization and coordination of various individuals, committees and support services that comprise the HRPP:

Organizational Chart for the Human Research Protection Program (HRPP)



E. RESPONSIBILITIES

1. INSTITUTIONAL OFFICIAL: The Medical Center Director for the NWIHCS is the Institutional Official (IO) and signatory official for the Federal-wide Assurance (FWA) and is ultimately responsible for all aspects of the oversight of the Human Research Protection Program (HRPP) at the facility. The Director ensures effective coordination by and among the various individuals, offices, committees and/or subcommittees that comprise the HRPP; educational opportunities are provided for IRB members, staff and researchers; and adequate space and resources are available to comply with federal regulations and guidelines that govern human subjects research. (VHA Handbook 1200.05)

The Medical Center Director on behalf of the NWIHCS grants the IRB the authority:

- a. To approve, require modifications to secure approval, or disapprove all research activities overseen and conducted by the organization.
- b. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants.
- c. To observe, or have a third party observe the consent process.
- d. To observe, or have a third party observe the conduct of the research.

The Medical Center Director and other officials of NWIHCS cannot approve research at the NWIHCS if it has not been approved by the IRB (subcommittee of the R&D Committee).

2. RESEARCH COMPLIANCE OFFICER: The NWIHCS maintains an institutional program to review issues relative to compliance and assurance of clinical research involving human subjects. This program is to comply with regulations requiring a HRPP. Authority and responsibility for this oversight activity, regulation and compliance resides in the Office of the Director, who also acts as the Institutional Official.

- a. The Office of the Director will initiate and direct regular audits by the Research Compliance Officer or other standing entities at the NWIHCS as appropriate of research activities to monitor both clinical and investigative performance including the actions of the IRB and R&D Committee. Specific activities will include:
 - 1) Monitoring of research activity such as observation of the informed consent process.
 - 2) The Research Compliance Officer will develop and conduct regular audits that monitor the consent process, protocols and Principal Investigator (PI) performance and compliance.
 - 3) Respond to specific requests for auditing and monitoring research activities from legislative and regulatory organizations.
- b. All results of the compliance audits will be reported to the IRB, R&D Committee, Chief of Staff and the Director, and appropriate external entities as required.

3. ACOS/RESEARCH & DEVELOPMENT PROGRAM OVERSIGHT: The ACOS/R&D assisted by the AO in conjunction with the R&D Committee are responsible for the operation of the research program, providing administrative support to and implementing the decisions of the R&D Committee and the IRB. The ACOS/R&D ensures the administrative structure is in place and

functioning effectively to carry out the research mission of the Medical Center and is in compliance with regulations. The ACOS/R&D provides advice and assistance to the R&D Committee and the IRB on administrative and regulatory matters and to investigators on both scientific and administrative matters, including the requirements for conducting research involving human subjects. The ACOS/R&D notifies investigators in writing when a research project can be initiated or continued after all applicable R&D Committee and its subcommittees' approvals. All VA Central IRB PI or site applications are signed by the ACOS/R&D prior to submission. The ACOS/R&D is assisted by the Research Administrative Office staff, including the AO, who supervises the day-to-day operations of the Research Administrative Office. The ACOS/R&D and AO are available to receive and respond to the investigators' questions, concerns and suggestions.

4. RESEARCH AND DEVELOPMENT COMMITTEE:

The R&D Committee may strengthen requirements and conditions, or add other modifications to secure R&D Committee approval or approval by a higher authority. The R&D Committee may not approve research which has been disapproved by the IRB. The R&D Committee must review the HRPP including appropriateness of the composition of the IRB in regards to volume and types of human research to be reviewed, support staff, credentialing and training, adequate resources, all protocols, subcommittee minutes, compliance reports, goals, quality improvement and has access to all IRB records. The R&D Committee and IRB forward names via the ACOS to the Medical Center Director for consideration to be new IRB members. The Executive Committee of the Medical Staff has oversight of the R&D Committee.

5. SUBCOMMITTEE OF HUMAN STUDIES (IRB): The Subcommittee of Human Studies (SHS), hereafter referred to as the Institutional Review Board (IRB) is a subcommittee of the Research & Development (R&D) Committee. It is the primary organizational unit charged with the responsibility of protecting the rights and welfare of all individuals, whether patient, employee, or volunteer, who participate as subjects in the VA research program. The VA Central IRB is the IRB of record for multi-site VA studies that are requested by ORD to be reviewed and overseen by the Central IRB. The Medical Center Director discharges this duty of complying with the requirements of the Common Rule and the FWA, and VHA Handbook 1200.05 to the IRB. It reviews and approves all research before it begins and continually monitors ongoing research through periodic reviews at time intervals appropriate to the degree of risk, by review of unanticipated problems and adverse events (both cumulative and individual), and by review of all proposed modifications affecting human use. If a research activity is disapproved by the IRB, the decision cannot be overruled by the R&D Committee or any higher authority; nor can the IRB members experience undue influence in their decisions to approve or disapprove research. The structure and responsibilities of the IRB are described in detail in the IRB Standard Operating Procedures. The Office of Research Administration, led by the ACOS, provides administrative support to the IRB.

6. HRPP STAFF: The HRPP staff will be responsible for duties outlined in the Standard Operating Procedures manual. A brief description of these duties involve interpreting regulations and providing instructional guidance to committee staff members and principal investigators; applying for and maintaining the Federal Wide Assurance (FWA); apprising the Institution of human subject updates;

coordinating outside audit and site visits such as FDA, ORO, NCCTG or ECOG, etc.; preparing for accreditation of the HRPP; overseeing committee functions; recordkeeping, monitoring mandatory education and credentialing requirements, initiating and monitoring ongoing research, and following reporting requirements within and outside the NWHCS. The HRPP staff are available to receive and respond to the questions, concerns and suggestions of the investigators and their research team members.

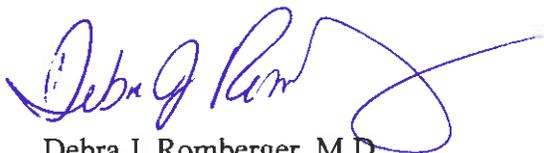
7. SPONSOR: The sponsor is the person or entity who takes responsibility for, or initiates a clinical investigation. The Omaha VA Medical Center seeks written assurances from sponsors via the CT CRADA that research is conducted according to applicable laws and regulations, good clinical practices and ethical standards. In agreements with sponsors, the VHA guidelines for Clinical Trial Cooperative Research and Development Agreements will be followed, including the explicit language regarding the protection of human subjects, dissemination of knowledge and health care to injured research subjects. The Human Research Protection Program and all VA statutes, regulations and policies at the Omaha VAMC will apply to sponsored research, as well as, all research conducted at the facility. Compliance activities are conducted in accordance with VA requirements.

8. PRINCIPAL INVESTIGATORS:

It is the responsibility of the Principal Investigator (PI) to initiate the application and be involved in all aspects of the research proposal including the design of the study, conduct of the study, analysis and interpretation of the collected data and writing of resulting manuscripts. The PI must have a VA NWHCS staff appointment: 1) compensated by the VA, 2) works under a WOC appointment initiated by his/her clinical service, or 3) be an employee assigned to the VA through the Intergovernmental Personnel Act of 1970.

F. HRPP Review:

The HRPP will be reviewed annually by the R&D Committee. The HRPP policy will be forwarded to the Chief of Staff and Medical Center Director for approval.

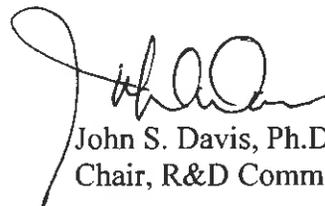


Debra J. Romberger, M.D.
ACOS/R&D

Concur:

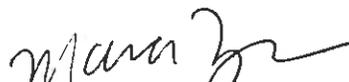


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