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## **HUMAN RESEARCH PROTECTIONS PLAN**

**Veteran Affairs Maryland Health Care System**  
(VAMHCS)

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ABBREVIATIONS

ACOS/R&D	Associate Chief of Staff for Research and Development
AO/R&D	Administrative Officer for Research and Development
BREF	Baltimore Research and Education Foundation
CIRB	Central Institutional Review Board
CITI	Collaborative Institutional Training Initiative
CAP	Corrective Action Plan
CFR	Consolidated Federal Register
CICERO	Comprehensive Institutional Evaluation of Research Online
CRADO	Chief Research & Development Officer
RCOIO	Research Conflict of Interest Officer
COS	Chief of Staff
CPRS	Computerized Patient Record System
DSMB	Data Safety Monitoring Board
DSMP	Data Safety Monitoring Plan
EPIC	Executive Performance Improvement Committee (VAMHCS)
FDA	Food & Drug Administration
FWA	Federalwide Assurance
GCP	Good Clinical Practices
HARPO	Human and Animal Research Protections Officer
HIPAA	Health Insurance Portability and Accountability Act
HRP	Human Research Protection (prefix to applicable R&D Service SOPs)
HRPO	Human Research Protection Office (UMB office that administers the IRB)
HRPP	Human Research Protection Program
II	Individually Identifiable Information
ICF	Informed Consent Form
IDMC	Impaired Decision-Making Capacity
IDS	Investigational Drug Service
IDP	Investigational Drug Pharmacist
IRB	Institutional Review Board
IRB P&P	Institutional Review Board Policies and Procedures
ISO	Information Security Officer
IT	Information Technology
MCD	Medical Center Director
MOU	Memorandum of Understanding
NOPP	Notice of Privacy Practices
OHRP	Office for Human Research Protections
ORC	Office of Research Compliance (VAMHCS)
ORD	Office of Research & Development (VA)
ORO	Office of Research Oversight (VA)
PI	Principal Investigator

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PO	Privacy Officer
QA	Quality Assurance
QI	Quality Improvement
QMP	Quality Management Plan
R&D	Research & Development
RCO	Research Compliance Officer
RCOIO	Research Conflict of Interest Officer
R&DC	Research & Development Committee
RDS	Research & Development Service
TMS	Talent Management System
SOP	Standard Operating Procedure
UMB	University of Maryland Baltimore
UPR	Unanticipated Problem Involving Risks to Participants or Others
VAMHCS	VA Maryland Health Care System
WOC	Without Compensation

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**I. Definition of the Human Research Protections Program and Mission Statement<sup>1</sup>**

The VA Maryland Health Care System (VAMHCS)<sup>2</sup> Human Research Protection Program (HRPP) is a comprehensive and organized program with dedicated resources to ensure the rights, safety and well-being of human volunteers participating in research. The objective of the HRPP is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human participants in research. The program accomplishes this through an integrated approach towards personnel (from research staff through institutional officials), research participants, policy-making (standard operating procedures and guidelines reflecting changes in regulatory requirements), implementation (education and operation), and evaluation (auditing, reporting, and amending). There are Memoranda of Understanding (MOU) between the University of Maryland and VAMHCS, and between VHA Central Office and VAMHCS, that delegate the University of Maryland Baltimore Institutional Review Board and the VA Central Institutional Review Board (CIRB) as IRBs for human subjects research conducted in the VAMHCS. Diagrams of the organizational structure and operational structure of the VAMHCS HRPP are found in Attachments 1 and 2 and are discussed in Section IV.

Documents such as the Belmont Report and the Declaration of Helsinki are the foundations for the ethical conduct of human subjects research, and the guidance provided in these documents is helpful in structuring a framework for a HRPP. These documents emphasize prospective protections of research participants (establishment of Institutional Review Boards for a protocol approval process, the informed consent process, and so on), which are essential in actualizing the ethical principles of beneficence, autonomy and justice.

The VAMHCS HRPP also emphasizes commitment to protections of research subjects through the enforcement of Good Clinical Practices (GCP) guidelines. Adverse events monitoring, continual quality improvement, compliance oversight and continuing education, all have application in the preservation of the ethical principles of beneficence, autonomy and justice throughout the entire research process.

In addition, the Department of Veterans Affairs is one of 17 Departments and Agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects (45 CFR 46, Subpart A, “The Common Rule”), 21 CFR 50 and 56 (where applicable), and all relevant academic affiliate policies and VA rules and policies set forth in writing in

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<sup>1</sup> References and applicable policy memoranda are located in Section XII

<sup>2</sup> The Baltimore and Perry Point VA Medical Centers, the Baltimore VA Rehabilitation & Extended Care Center and a number of community based outpatient clinics (CBOC) in Maryland all work together to form this comprehensive health care delivery system.

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VHA Handbooks 1200.01, 1200.05, 1058.01, and other VHA handbooks as applicable. The Veterans Affairs Maryland Health Care System (VAMHCS) implements the requirements specified in 38 Code of Federal Regulations (CFR) 16, Protection of Human Subjects as well as additional VA-specific regulations: 38 CFR 17.33 (on patients rights), 38 CFR 17.85 (on treatment of research-related injuries to human subjects), 38 CFR 17.45 (on medical hospital care in research studies), and 38 CFR 17.92 (on outpatient care for research studies).

It is the mission of the VAMHCS R&D Service to produce research of high scientific quality for the benefit of the U.S. armed services veteran population in particular and for society as a whole, while protecting human participants' rights and safety.

The VAMHCS HRPP consists of the activities, policies and procedures of the VAMHCS, the University of Maryland, Baltimore (UMB) Human Research Protections Office (HRPO), UMB Institutional Review Board (IRB), the CIRB, the VAMHCS Research & Development (R&D) Service, and the individuals, committees and subcommittees who act on them. The “program” is not a document but a dynamic process of education, oversight, and action on human subjects protections that is codified in our policies and procedures.

This document, the “VAMHCS Human Research Protection Plan” (HRP 01.02), is a summary of the multi-faceted approach that has evolved within the VAMHCS research program. The purpose of this document is to give an overview of the VAMHCS Human Research Protections Program. For details of specific activities, it is necessary to refer to the policies, procedures and documents that are cited throughout this document.

### **A. Definition of Human Participant**

The VHA defines **Human Subject\*** as<sup>3</sup>:

A human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual or (2) identifiable private information. Individuals who receive test articles or who serve as controls in clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are also considered human subjects for the purposes of this Handbook..

(\*The VAMHCS uses the term “human participant” rather than “human subject” to be compatible with the IRB, Department of health & Human Services [DHHS], FDA, and Health Insurance Portability and Accountability Act [HIPAA] terminology.)

This definition is compatible with the HRPO definition, which is based on the DHHS and

<sup>3</sup> VHA Handbook 1200.5 §4.1

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FDA definitions:

According to DHHS, a **human participant** is a living individual about whom an Investigator (whether professional or student) conducting research obtains either: data through intervention or interaction with the individual or identifiable private information. These individuals could be patients, healthy volunteers, students, employees, and/or members of the community.

- **Interaction:** Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or the participant's private identifiable information.
- **Intervention:** This includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.
- **Private Information:** Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, medical records). Private information must be individually identifiable (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human participants.

For FDA regulated research, a human participant is an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be either a healthy individual or a patient.

The FDA further defines “human subject” as an individual on whose specimen a device was used.

With regard to HIPAA-applicable issues, the definition of “human” extends to the use of decedent's protected health information.

## **B. Definition of Research**

VA defines “research” as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of VA policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are considered research for purposes of VHA Handbooks<sup>4,5</sup>.

<sup>4</sup> Research activities are further discussed in VHA Handbook 1058.05.

<sup>5</sup> VHA Handbook 1200.5 §4.aa

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The following guidelines apply: “systematic” defined as “having or involving a system, method, or plan”, “investigation” defined as “a searching inquiry for facts; detailed or careful examination” and “generalizable knowledge” defined as as knowledge that is “universally or widely applicable”.

VA research is research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have R&D Committee approval.

In practice, the VAMHCS has delegated to the UMB IRB the determination of whether the activities constitute “research” involving “human subjects” as defined by FDA, DHHS, and VHA.

An activity is FDA-regulated research when:

- It involves any use of a drug other than the use of an approved drug in the course of medical practice. (21 CFR 312.3(b)) This is the meaning of “experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act” in the definition of “clinical investigation”.
- It evaluates the safety or effectiveness of a medical device (21 CFR 812.2(a)) This is the meaning of “experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act”.
- The results of the activity are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

DHHS defines **research** as:

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

### **C. Research Conducted, Prohibited or Restricted at the VA**

The VAMHCS conducts clinical, biomedical, social behavioral, genetic, epidemiology, chart review and database studies.

VAMHCS research is research that is conducted in VAMHCS facilities, is conducted in approved off-site locations/facilities, uses VA identifiable data, medical records or databases, otherwise uses VA resources, and/or is conducted by VAMHCS researchers while on official duty. The research may be VA funded, funded from extra-VA sources, or conducted without direct funding.

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Projects may be investigator-initiated or federally-funded or privately funded and may involve multiple sites. Research may involve students (as faculty-supervised investigators or as participants<sup>6</sup>), employees, and the secondary use of data, tissues or other biological specimens (including banked tissues).

Because the VAMHCS research program strives to conduct research that is relevant to the veteran population, veterans themselves, their family members and children are potential participants. The general population may also be recruited. Persons will be recruited without regard to gender, race or ethnicity unless the IRB approves restrictions that are cogent to the research being conducted. It is possible that vulnerable populations such as students, employees, persons with impaired decision-making capacity (IDMC), children and prisoners may be recruited. However, IRB-approved and R&D Committee-approved protections must be in place, as well as Chief Research & Development (CRADO) waivers if applicable.

The following categories of research are prohibited at the VA:

- Projects involving fetuses, *in utero* or *ex utero* (including human fetal tissue)
- Projects involving *in vitro* fertilization
- Projects involving embryonic stem cells
- Research that is “planned emergency research” such that the investigator is seeking a waiver of prospective informed consent
- Projects involving a recruitment strategy that requires “cold calls” to veterans and/or asking veterans for social security numbers during a phone call
- “Recruitment-only” protocols.

The following categories of research require special criteria and must obtain a CRADO waiver or MCD approval in order to be conducted at VA<sup>7</sup>:

- Research involving children as research subjects (MCD approval)
- Research involving prisoners as research subjects (CRADO waiver)
- International research (MCD approval)
- Research involving pregnant women, human fetuses and neonates as research subjects (MCD approval)
- Subjects lacking decision making capacity.

<sup>6</sup> Trainees (e.g., students, residents fellows of any profession), may serve as participants, but not PIs within a VA facility, use VA human subjects data, or use human biological specimens that have been collected within VA for clinical, administrative, or research purposes only when: (1) The study has been approved by the local VA medical facility and IRB, if appropriate; and (2) Either they are: (a) Enrolled in an institution with an educational affiliation agreement with that VA facility; or (b) Directly appointed to a VA training program that has no external institutional sponsorship (e.g. VA Advanced Fellowship). NOTE: A waiver may be obtained from the CRADO under special circumstances. [VHA HB 1200.05, §28] Similarly, UMB does not allow students or fellows to be principal investigators. Further information on the conduct of research by UMB-affiliated students or other trainees at the VAMHCS is available in the UMB “Investigator Manual” available at the HRPO website: <http://www.hrpo.umaryland.edu/default.asp>.

<sup>7</sup> VHA Handbook 1200.05 §17, §18, §19, §20, §26

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The VAMHCS does not conduct classified research.

## II. Policy<sup>8</sup>

1. VAMHCS investigators, staff and sponsors must place the health, safety and rights of human participants as their top priority in the conduct of their research. This includes consideration of the underlying ethical principles of beneficence, autonomy, and justice (see II.A below). Investigators must conduct their research according to the protocols and procedures approved by their Department Chairs/Service Chiefs, the IRB and the R&D Committee (R&DC). VAMHCS investigators and staff follow HRPO Policies and Procedures unless additional VAMHCS requirements exist. VAMHCS researchers must adhere to all applicable VA and other federal requirements.

Sponsors are similarly bound, through their agreements with the VAMHCS, to follow accepted ethical obligations as well as HRPO/CIRB policies and VAMHCS HRPP requirements.

2. It is the policy of the VAMHCS that the IRBs have the authority to approve new protocols and protocol modifications and conduct continuing review. The IRBs also make the determination as to whether a research proposal is “human subjects research”, whether the VAMHCS is engaged in research (and VAMHCS staff are therefore “agents” in research activities), whether a research proposal meets criteria for “exempt from applicable federal, state and local regulations“ or is eligible for expedited review, the validity of Investigational new Drug (IND) and Investigational Device Exemption (IDE) numbers or decisions about IND and IDE exemptions, emergency use of test articles, and suspension and termination of studies. With regard to engagement in research, the R&D Committee makes final decisions on “without compensation (WOC) status for VAMHCS research.
3. When making determinations on the “exempt” status of research projects, the IRB also determines whether the exempt study meets ethical standards. The R&DC must also consider the ethical standards of VAMHCS research that has been determined to be exempt by the IRB.
4. The R&D Committee may only approve or disapprove research that has been approved by the IRB or determined exempt by the IRB. The R&D Committee may disapprove research for the VAMHCS that has been approved by the IRB

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<sup>8</sup> References and applicable policy memoranda are located in Section XII.

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- and must notify the IRB if this occurs (the research could proceed at UMB but not in any way that could engage the VAMHCS in the research). Research reviewed and approved by the IRB may be subject to review and disapproval by the Medical Center Director (MCD) or other institutional officials. The MCD and institutional officials may not approve research not approved by the IRB or the R&D Committee (i.e., decisions may not be more lenient than those of the IRB). The R&D Committee must notify the Associate Chief of Staff for R&D (ACOS/R&D) of decisions regarding approvals and disapprovals of research.
5. For “collaborative studies” in which some parts of the research project are conducted at the VAMHCS or use VA resources, and other parts are conducted at the collaborator’s institution, The VAMHCS R&D Committee (R&DC) only approves the VA portions of the project. The VAMHCS MCD is the Institutional Official (IO) for the VA portions of the study.
  6. All licensed research staff that perform research activities within VAMHCS space or on VAMHCS paid time, under a license, registration or certification must be credentialed through the Department of Veterans Affairs (VA). All research staff (licensed or unlicensed) who perform research activities within VAMHCS space or on VAMHCS paid time must also have a Research Scope of Practice Statement signed by the ACOS/R&D. The Research Scope of Practice Statement must clearly define the parameters or functions that are allowed or not allowed to be performed as part of the duties of these individuals.

### **A. Ethical Principles Concerning the Protection of Human Research Participants**

In 1979, the Belmont Report asserted that there are “three basic ethical principles among those generally accepted in our cultural tradition, [that] are particularly relevant to the ethics of research involving human subjects: the principles of respect of persons, beneficence, and justice.”

Respect for persons was further clarified:

Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

Beneficence was regarded as a strict obligation to (1) do no harm, but also to (2) maximize possible benefits and minimize possible harms. The principle of justice struggles with the question of “who ought to receive the benefits of research and [who ought to] bear its burdens.”

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The Belmont Report further advanced the evolution of human subject protections by devoting a large section to practical applications of these ethical principles to the conduct of research. In particular, it discussed three requirements that had already been codified in the Declaration of Helsinki and in Federal regulations (FDA, DHHS) and demonstrated how beneficence, autonomy and justice could provide a framework for procedural or programmatic decision-making with regard to human research programs.

Its discussion of informed consent emphasized the *process* rather than the written consent form as a way of promoting autonomy and beneficence. It specifically instructed that the process should contain three elements: information, comprehension and voluntariness.

The VAMHCS considers the Informed Consent Form (ICF) as a tool for informing potential subjects about a study and for documenting their consent. It has implemented the use of supplemental tools such as the “Informed Consent Form Checklist”, “Informed Consent Process Worksheet”, tests for mental or decisional capacity, tests for understanding (ICF post-tests, etc.) and, most importantly, a process of discussion, questions & answers, deliberation, and other personal interchanges between the potential participant and the study staff (including the PI) as a way to shift the focus of research staff from a signed form to the quality of the process.

Through its designated Institutional Review Boards (the UMB IRB and the VA CIRB) and the VAMHCS R&DC, the VAMHCS ensures that informed consent forms contain essential elements of informed consent (and additional elements, as applicable), that protocols are assessed for risks, benefits, and scientific merit, that potential conflicts of interest are examined and minimized, and that subject selection is not burdensome to vulnerable/minority groups. The VAMHCS R&D Service ensures that the VAMHCS research policies are in compliance with applicable sections of the VHA Handbook 1200.01 (R&D Committee), VHA Handbook 1200.05 (Human Research Protections), VHA Handbook 1108.4 (Investigational Drugs), VHA Handbooks 1605.1 and 1605.2 (PHI and privacy), VHA Handbook 1058.01 (Research Compliance), the Common Rule, and other applicable Veterans Administration, federal and state regulations.

The rights and autonomy of research participants are further protected by the Institution’s development and implementation of HIPAA-compliant and VHA-compliant privacy policies and procedures. Data Safety Monitoring Plans (DSMPs) are one aspect of the IRBs’ and VAMHCS goal of preventing harm to study participants.

The principles of beneficence, autonomy, and justice are essential tools as the VAMHCS R&D Service develops programs of quality assessment and improvement, mandates innovations in the procedures by which protocols are approved and conducted, and makes decisions on investigator compliance.

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### B. Engagement in Research and Assurances

It is the responsibility of the VAMHCS to formally “assure” the VA and other federal agencies in writing that, when engaged in research, it will comply with regulations governing the protection of human subjects. The VAMHCS MCD is the Assurance Signatory/IO and is ultimately responsible for overseeing the protection of human subjects within the facility. The Institutional Official must also ensure that open channels of communication are maintained between the IRBs, research investigators and staff, and facility management.

A VA **facility** is **engaged** in human subject research (and needs an Assurance) whenever its **employees** or **agents**:

- Intervene or interact with living individuals for research purposes, *or*
- Obtain, release, or access individually-identifiable private information (or individually-identifiable specimens) for research purposes. [38 CFR 16.102(f)]

This is further clarified in an Office of Research Oversight (OHRP) Guidance (Jan 1999) as well as in IRB policies and procedures (P&P). A person or institution is **engaged in research** when:

- The person intervenes with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood; collecting other biological samples; dispensing drugs; administering other treatments; employing medical technologies; utilizing physical sensors; utilizing other measurement procedures).
- The person intervenes with living individuals by manipulating the environment for research purposes (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; orchestrating environmental events or social interactions; making voice, digital, or image recordings).
- The person interacts with living individuals for research purposes (e.g., engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent).
- The person releases, obtains, receives, or possesses private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes (e.g., obtaining private information from medical records and/or research records in an individually identifiable form).

An “**agent**” of the VAMHCS is:

Anyone with an appointment to the VAMHCS, whether they are an employee or a WOC appointee, and who is engaged in research for the VAMHCS.

### C. Arrangements for an Institutional Review Board (IRB)

The VAMHCS has designated the UMB IRB and the VA CIRB as its IRBs of record and has established MOUs delineating the responsibilities of the UMB, the CIRB, the

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VAMHCS and the Baltimore Research & Education Foundation (BREF). The UMB IRB has agreed to comply with 38 CFR 16 and applicable VHA handbooks when reviewing VA research.<sup>9</sup> The VA prohibits the use of commercial IRBs.

UMB maintains a Federalwide Assurance (FWA) with DHHS OHRP (#FWA 00007145). Six IRBs at UMB are linked to this assurance.<sup>10</sup> Each of the six IRBs reviews VA research protocols. IRB 1 is the currently active IRB at this time.

The VA CIRB maintains an FWA with OHRP (FWA00013518).

The VAMHCS maintains FWA # 00001483 registered with OHRP via the Office of Research Oversight (ORO).

The BREF, the VAMHCS non-profit foundation, maintains an FWA with OHRP (#FWA 00001420).

The VAMHCS strives to comply with federal statutes governing the VA (38 CFR 16 and 38 CFR 17), DHHS and FDA regulations, and VHA Handbooks. As a federal agency it is exempt from PHS and other federal agencies' regulations. The VAMHCS also complies with UMB HRPO and CIRB policies and procedures. The HRPO recognizes that there are VA-specific requirements that VAMHCS staff and IRBs are obligated to follow. These VA requirements have been incorporated into HRPO policies and procedures where applicable. The UMB HRPO policies and procedures comply with DHHS, FDA, PHS regulations and Maryland state law. Where conflicts occur, the stricter standard will be followed. The UMB Legal Counsel and/or the VA Regional Counsel will be consulted when necessary for guidance in applying laws within the state of Maryland and outside the state of Maryland to research involving human participants.

#### **D. HRPP Document and Related Standard Operating Procedures**

This document, the “VAMHCS Human Research Protection Plan” (HRP 01.02), summarizes the VAMHCS program of research oversight and human subject protection. Instead of giving lengthy operational detail for carrying out these functions, it refers the reader to VAMHCS R&D Service Human Research Protection (HRP) Standard Operating Procedures (SOPs), VAMHCS R&D Service Process Modules (PM), IRB policies & procedures, and other documents.

This particular document (HRP 01.02) and the SOPs and guidelines referenced herein are on three year review cycles. However, all HRP documents are subject to early review or amendment as necessitated by institutional or regulatory changes.

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<sup>9</sup> See IRB P&P.

<sup>10</sup> IRB numbers: 00000233, 00000234, 00000235, 00002923, 00006045, 00007347

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### **III. Identification of the Institutional Officer Accountable for the HRPP**

The MCD is the Institutional Official (IO) and is therefore accountable for the implementation and performance of the HRPP. He is the Institution's signatory on the FWA and MOUs.

### **IV. The Organizational Structure, Process, Roles and Responsibilities for Making Policies to Protect Human Research Subjects<sup>11</sup>**

#### **A. Organizational Structure: Responsibilities**

The organizational structure of responsibilities for the VAMHCS Human Research Protection Plan is diagrammed in Attachment 1. This chart specifically selects out individuals or offices that have HRPP-related functions and is not meant to be an illustration of the entire organizational structure of the VAMHCS R&D Service.

While the MCD has ultimate accountability for the HRPP, the Human & Animal Research Protections Officer (HARPO) through the ACOS/R&D and Chief of Staff (COS), is the Director's designee for the implementation of the HRPP. The following VAMHCS entities are integrally involved with the performance of the HRPP: Research & Development Service, the R&DC, the Subcommittee on Research Safety, the Radiation Safety Officer, the Privacy Officer, the Information Security Officer, the Investigational Drug Service, the Office of Research Compliance (ORC), and the UM IRB and CIRB.

The MCD is ultimately responsible for VA oversight of the UM IRB, the R&D Service (through the COS), the R&DC (through the COS) and VAMHCS investigators. Neither the MCD nor any VAMHCS individual or committee may approve a research project that has not been approved by the IRB and the R&DC.

#### **B. Organizational Structure: Process**

While ultimate responsibility for the HRPP rests with the MCD, most of the development, education, implementation and compliance assessment takes place within the R&D Service. This is illustrated in the flowchart in Attachment 2.

As illustrated in Attachment 2, the HRPP Program, administered by the HARPO is the central point of action for the non-audit portions of the VAMHCS HRPP. The HARPO reports directly to the ACOS/R&D. The ORC conducts the audit program mandated by

<sup>11</sup> References and applicable policy memoranda are located in Section XII.

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ORO. The ORC is administered by the Research Compliance Officer (RCO) who reports directly to the MCD and is independent of the R&D Service.

The policies and procedures that the HARPO develops are influenced by policies, regulations, guidance and correspondence from VHA Office of Research Oversight (ORO), VHA Office of Research & Development (ORD), OHRP, the FDA, accreditation entities and other applicable external agencies. The VAMHCS ORC communicates findings from audits and other feedback to the R&D Service. The HARPO obtains additional feedback through investigations of complaints and allegations of noncompliance, and through related communications with ORO, accrediting agencies, oversight visits, etc.

R&D Service policies and procedures implement the requirements specified in 38 CFR 16, 38 CFR 17, VHA Handbooks, and IRB P&Ps. As policies are developed, amended or renewed, the HARPO submits them to R&D Service leadership, R&DC Chair(s), and other vested parties for review and guidance. The R&DC is notified of ACOS/R&D-approved SOPs and process modules (PM). The new or revised SOPs and PMs are reported to the R&DC and are included in R&DC meeting minutes. The MCD is notified of new or revised SOPs and PMs through attendance at R&DC meetings and through minutes.

For VAMHCS research under the purview of the UM IRB, VAMHCS researchers and staff must follow UMB policies and procedures unless explicitly stipulated in IRB policies and procedures (IRB P&P). The HARPO collaborates with the UMB HRPO to ensure that IRB P&P are compatible with and include all applicable VA regulations and VAMHCS requirements.

For VAMHCS research under the purview of the CIRB, researchers and staff must follow applicable CIRB policies & procedures.

Once policies are approved or modified, education of VAMHCS investigators, coordinators and staff begins. This is achieved through the “Research Service Hot Topics” series, “Brown Bag” meetings, presentations, emails, web-based training, manuals, and other methods. Investigators are responsible for ensuring that their research team is aware of VAMHCS policies & procedures and that the policies and procedures are then implemented in their research units or for individual protocols. Hot Topics approved by the ACOS/R&D are also used as bridge PMs or SOPs when necessary. R&D Service SOPs, Hot Topics archives, and other useful information are accessible through the R&D Service website, [www.maryland.research.va.gov](http://www.maryland.research.va.gov).

The HARPO also serves as a resource for investigators and their staff. The HARPO assists them in the development of their own internal policies and procedures and in self-assessments of their own programs. The HARPO also provides guidance and consultation to research personnel and VAMHCS leadership.

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The ORC performs informed consent form audits and triennial regulatory audits as mandated by ORO. The ORC currently provides audit reports to the IRBs, R&DC and PI. The ORC reports any assessments of “apparent serious or continuing noncompliance” to the IRB and ORO. The IRB makes final determinations of serious and/or continuing noncompliance.

At this time, it is the HARPO that follows up on corrective action plans and updates to ORO, IRB and R&DC, and, if necessary, OHRP. The HARPO also ensures notification of the IRBs for any apparent serious or continuing noncompliance not found through ORC audits.

As mandated by VHA Handbook 1200.01, the VA R&DC performs regular (at least annual) assessments of the VAMHCS HRPP, the UMB HRPO and the R&D Service itself. This includes evaluations of the performance of the VAMHCS designated IRBs (UMB and VACIRB), UMB IRB compliance with VAMHCS policies, relevance and accuracy of VAMHCS and R&D Service policies, and performance of the R&DC and its subcommittees. The goal of these assessments is to determine whether these entities are effective in achieving their intended outcomes. The results from these evaluations are used to design and implement improvement plans that are relevant to the needs of the organization.

Representatives of the R&D Service or ORC may periodically present educational sessions on VA research matters to the IRB and R&DC and subcommittee members.

### C. Roles

The following are agents of the VAMHCS’ research program.

1. The Medical Center Director: The Medical Center Director (MCD) is the VAMHCS Institutional Official and, as such, is responsible for ensuring that the institution’s HRPP functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects, and for fostering an institutional culture that supports ethical conduct of all research involving human subjects. This involves the oversight of the HRPP, the IRBs and overall research program.
  - a. As delineated in VHA Handbook 1200.05 these responsibilities include:
    - (1) Overseeing the R&D Committee, IRB, and other applicable subcommittees of the R&D Committee, facility research office, and all VA investigators and VA research staff who conduct human subjects research at that facility.
    - (2) Delegating authority in writing for respective roles and responsibilities for the HRPP. This delegation of authority must provide the organizational structure and

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- ensure leadership for oversight activities for all human subjects research conducted at or by the facility.
- (3) All research subject to this Handbook [1200.05] must be reviewed and approved by an IRB designated in the facility's FWA (the IRB of Record), and will be subject to continuing review and oversight by the IRB of Record.
- (4) The IO is responsible for ensuring that any IRB designated as an IRB of Record for the facility is established in accordance with the requirements of this Handbook [1200.05] and registered through the [sic] ORO to the Office for Human Research Protections (OHRP).
- (5)
- ~~(1)~~(6) Ensuring that any IRB designated as an IRB of Record for the facility is established in accordance with the requirements of this Handbook and registered through the ORO to the Office for Human Research Protections (OHRP).
- ~~(2)~~(7) Appointing in writing at least two VA-compensated (minimum 1/8th full-time employee equivalent) staff from the facility are appointed as voting members to each IRB of Record except for the VA Central IRB.
- ~~(3)~~(8) For research involving pregnant women, human fetuses, and neonates as subjects, certifying that the medical facility has sufficient expertise in women's health to conduct the proposed research
- ~~(4)~~(9) For research involving children, approving participation in the proposed research based on the project's relevance to VA and that it is greater than minimal risk
- ~~(5)~~(10) Approving participation in international research
- ~~(6)~~(11) Ensuring necessary medical treatment to a research subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees.
- ~~(7)~~(12) Ensuring provision of adequate resources to support the operations of HRPP so that those operations are in compliance with all VA and other Federal requirements that govern human subjects research protection.
- ~~(8)~~(13) Ensuring independence of the IRB;
- ~~(9)~~(14) Ensuring that a procedure is in place to review and approve recruiting documents, flyers, and advertisements for research that is not VA research prior to being posted or distributed in any form within or on the premises of a VA facility. Posting or distributing may include announcing, distributing, publishing, or advertising the study either electronically, by hard copy, or other means to anyone, including Veterans, clinicians, or other staff (see ORD guidance at <http://www.research.va.gov/resources/policies/default.cfm>).
- ~~(10)~~(15) Ensuring that IRB members, R&DC 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.
- ~~(11)~~(16) Being the point of contact for correspondence addressing human subjects research with OHRP, FDA, and VHA Central Office;
- ~~(12)~~(17) Ensuring the VA facility's HRPP is accredited by an organization approved by ORD to perform this function.

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- b. As delineated in VHA Handbook 1200.01, the MCD is a non-voting member of the R&DC and is responsible for:
- (1) The facility's research program, and is assisted by an R&DC. The MCD serves as the Institutional Official responsible for all aspects of the research program including but not limited to: human subjects protection, animal welfare care and use, privacy and security of VA data, and biosafety.
  - (2) Ensuring that research in which the facility is engaged is approved by the appropriate R&DC subcommittees.
  - (3) Ensuring there are adequate resources and administrative support, including personnel, space, equipment, and training, for the R&DC and its subcommittees to fulfill their responsibilities.
  - (4) Ensuring appropriate education and training for members of the R&DC, the research administration staff, and other staff involved in research.
  - (5) Ensuring that investigators meet the requirements stated in VHA Handbook 1200.01.
  - (6) Appointing the members of the R&DC following the specifications in VHA Handbook 1200.01.
- c. As delineated in VHA Handbook 1058.01, the MCD is responsible for:
- (1) Fostering a culture of accountability and transparency relative to research compliance;
  - (2) Ensuring that local SOPs are developed and implemented to implement effectively the requirements of all applicable VA and VHA Directives and Handbooks, including requirements pertinent to the facility's academic affiliate(s); and Provide for timely and effective communications among all components of the research program, the research review committees, and other relevant offices and committees (e.g., environmental management, human resources, police service, radiation safety committee).
  - (3) Reporting to ORO in the timeframes specified in VHA Handbook 1058.01, any situation that is reportable to ORO under VHA Handbook 1058.01,
  - (4) Ensuring timely implementation of remedial actions in response to identified noncompliance or as otherwise found warranted by ORO;
  - (5) Completing the annual VA facility Director Certification of Research Oversight.
  - (6) Appointing one or more RCOs to conduct annual research informed consent audits and triennial regulatory audits, and to assist in facility assessments of regulatory compliance. The lead RCO must report directly to the MCD and RCO activities may not be determined or managed by the R&D Service, research investigators, or any other research personnel.
  - (7) Reporting any RCO appointment, resignation, or substantive change in duties to ORO within 5 business days after the action takes effect.
  - (8) Ensuring that all research compliance reports from any State or Federal oversight entity (including ORO), regardless of findings, are provided to the ACOS/R&D, the R&D Committee, any other relevant research review committees, and the RCO within 5 business days after receipt.
- d. As delineated in VHA Handbook 1058.03, the MCD is responsible for:

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- (1) Serving as the IO and signatory to FWA and is therefore responsible for the Facility's compliance with all federal and VA research oversight requirements;
- (2) Completing all required trainings related to the duties of Institutional Officials for Federal-wide (Human Subject) Assurances (FWAs).
- (3) Signing new, renewing and revised VA FWA Addenda prior to approval by OHRP, with notification to ORO.
- (4) Signing new, renewing and revised memoranda of understanding (MOUs) documenting pertinent roles and responsibilities relative to the designation of another entity's IRB as a VA medical facility's IRB of Record.
- (5) Establishing an R&D Committee to conduct oversight of its human research program.
- (7) Ensuring that R&D Committee members have sufficient experience and/or training to conduct oversight of human research.

**e.** Other MCD responsibilities include:

- (1) Is responsible for ensuring compliance in research with all requirements for: protection of human research subjects, care and use of laboratory animals, research laboratory safety, including safety of research laboratory personnel and others, safety and control of infectious agents, safety and control of radioactive materials, safety, control, and security of other hazardous agents, safety, control, and security of designated "select" agents and toxins, granting access to research areas in which hazardous agents are used or stored, research involving recombinant DNA (rDNA), security against terrorist events, research information protection, including information security and privacy.
- (2) Is responsible for all required reporting to and correspondence with Federal oversight offices and agencies, and applicable accreditation organizations;
- (3) Ensures the appointment of: Permanent Research Integrity Officer (RIO) for Research Misconduct, Research Misconduct Inquiry/Investigation Committee members, Radiation Safety Officer, Research Safety Coordinator, Biological Safety Officer (rDNA program).
- (4) Ensures that the Facility maintains (a) all required programs, plans, and standard operating procedures (SOPs) for research compliance; and (b) documentation that these programs, plans, and procedures are current, accurate, and complete: HRPP, Research Participant Outreach Program, Animal Care and Use Program (ACUP), Research Safety and Security Program (RSSP), Research Information Protection Program (RIPP), Chemical Hygiene Plan, Hazardous Agents / Select Agent Control Program, Safety (Biosafety) Plan (Research Service-Wide Safety Manual), Security Plan (Site-Specific), Emergency Preparedness and Incident Response Plan, Personnel access to select agents or toxins approval by the Animal and Plant Health Inspection Service (APHIS) or the Centers for Disease Control and Prevention (CDC) based on Security Risk Assessment, all Other Facility Safety Programs (cover all research personnel and research space), R&D Service Education Plan, Animal Facility Disaster Plan, SOPs for Financial Conflicts of

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- Interest in Research, R&DC, the IRB, the IACUC, the SRS, other R&D Subcommittees..
- (5) Ensures that (a) all Facility research personnel have received required research compliance training, and (b) all training and credentialing requirements have been documented for: all research investigators and study coordinators, laboratory animal personnel (where applicable), relevant administrative staff, and relevant support staff, all licensed or unlicensed physicians or other professionals, ACOS/R and Administrative Officer for Research (AO/R), R&DC and applicable Subcommittee members (e.g., IRB, IACUC, SRS), RIO (and Research Misconduct Inquiry/Investigation Committee members as needed), Research Compliance Officer, all persons administering, working in, or (as warranted) visiting research areas.
  - (6) Ensures that he (a) performed the required review of annual and/or semi-annual program assessments and other research oversight reports; (b) submitted all required reports to oversight and accreditation agencies; and (c) implemented Action Plans to remedy any identified noncompliance by the Facility with federal or VA research oversight requirements: verification that all research involving sensitive or protected information has been reviewed by the IRB, PO, and/or ISO, verification that all research databases are compliant with Federal Information, processing Standards (FIPS) and VA Information Technology (IT) standards, verification that all laptops used for research are encrypted and compliant with FIPS and VA IT standards, submission in a timely fashion of all required reports to oversight and accreditation bodies.
  - (7) Ensures that the R&DC and its subcommittees, including its IRBs, function independently and without undue influence;
  - (8) Is available to R&DC or subcommittee chairs, co-chairs or members if they experience undue influence or if they have concerns about the R&DC or IRB;
  - (9) Delegates authority to one or more individuals to 1) provide comments or suggestions to CIRB in response to CIRB's initial review considerations, 2) respond to VA CIRB's approval of the study on behalf of the VAMHCS as to whether the VAMHCS chooses or declines to participate in the study, 3) serve as a liaison between the VAMHCS and both local site researcher and CIRB

2. The Chief of Staff:

- Oversees R&D Service functions;
- Meets regularly with the ACOS/R&D and/or Deputy ACOS/R&D on activities of the R&D Service;
- Receives reports from the Executive Committee of the Medical Staff, the ACOS/R&D, and the R&DC;
- Reports to the MCD;
- Is a non-voting member of the R&DC.

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3. The Associate Chief of Staff for Research (ACOS/R&D) is responsible for management of the research program. Specifically, the ACOS/R&D is responsible for:
- The ethical conduct of VAMHCS research, including the protection of human subjects, the care and use of animals, and the safety of research personnel;
  - Administration of the facility's R&D program, including the operations of the R&DC and subcommittees;
  - Participation with the MCD in the management of the facility's health care programs, particularly in those areas where integration of the R&D programs can have a beneficial effect on patient care;
  - Assisting investigators by providing advice and guidance in administration and technical matters;
  - Notifying the investigator when a research project can be initiated. This notification occurs only after the research project has been approved by all applicable R&DC subcommittees, and after the R&D subcommittees' notifications of approvals have been approved by the R&DC. The ACOS for R&D is responsible for notifying the investigator of approval after continuing review by the R&DC and subcommittees.
  - Functioning as Executive Secretary of the R&DC;
  - Is a non-voting member of the R&DC;
  - Aiding in the recruitment, appointment, and employment of R&D personnel; the progress review of investigators' R&D programs;
  - Ensures notification of VHA Office of R&D when research results are accepted for publication in a scientific journal, presentations are scheduled involving a national venue or the media, media interviews are scheduled, or professional activities are scheduled or known that involve a national venue or formal recognition;
  - Ensuring that information pertaining to all requests for WOC appointments for research have been appropriately justified and the appointments are in compliance with all applicable research, Human Resource Management, and other VA policies;
  - Providing an annual quality assurance review of research employees involved in human subject research to ensure the employees are working within their scopes of practice and their privileges allowed by the facility's by-laws and granted to them by the facility;
  - Providing an annual quality assurance review of Cooperative Research and Development Agreements (CRADAs) and other agreements in support of the research program or specific research projects and an assessment of the impact of these agreements on the research program, when applicable;
  - Ensuring that all minutes of the R&DC and its subcommittees, including those from subcommittees at VA facilities or at the affiliate, are sent to the MCD and COS for review and appropriate action;
  - Ensuring dissemination of educational materials to all investigators with active or planned research programs, to R&D Service personnel, and to R&DC members and subcommittee members (IRB, SRS, IACUC);
  - Preparation, submission, and maintenance of communications, reports, and correspondence required for the administration of the facility's R&D program;

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- Financial management of the facility’s R&D program.
  - Supervision of contracts when requested
4. The Deputy Associate Chief of Staff for Research (Deputy ACOS/R&D) assists the ACOS/R&D in the management of the VAMHCS research program. The Deputy ACOS/R&D:
- Assists the ACOS/R&D in interactions with medical center leadership, medical school leadership (UMB School of Medicine), VA Central Office, and other external bodies as needed;
  - Systematically reviews and reports on such administrative functions as manpower utilization, personnel, training, space utilization, supply procedures, and reports;
  - Administers the research grant review and submission process for VA funding, including the grants support staff;
  - Has supervisory responsibilities for management of research laboratories, including the chemical hygiene program, research safety, space and infrastructure concerns, etc.;
  - Is a non-voting member of the R&DC;
  - Performs other related functions as assigned by the ACOS/R&D.
5. The Administrative Officer for Research & Development (AO/R&D) is responsible for:
- Preparing and revising long-range plans for personnel, equipment, space, and construction requirements;
  - Develops and implements control procedures for fiscal matters, supplies, equipment, and services such as common resources and animal facilities;
  - Manages R&D contracts, including initiation, tracking, and implementation of the contracts;
  - Planning construction and minor alterations;
  - Maintaining inventory records of non-expendable equipment;
  - Assembling, organizing, and presenting information for budget preparation;
  - Attends the Institution’s budget hearings with requests for support of HRPP and other R&D Service programs;
  - Presents the Institution’s Chief Financial Officer with requests for funding;
  - Reports the budget analysis to the R&DC at least annually;
  - Assisting such administrative functions as recruitment of staff, personnel actions, preparation of reports by investigators, provisions of facilities for the R&DC and its subcommittees, and preparation of reports by the ACOS/R&D;
  - Supervising nonprofessional R&D Service administrative staff members;
  - Is a non-voting member of the R&DC;
  - Performing other related functions as assigned by the ACOS/R&D.
6. The Human and Animal Research Protections Officer (HARPO) is responsible for policies and accreditations of the VAMHCS research program, and education of the VAMHCS research community.

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- Uses subject matter expertise to develop, implement and evaluate VAMHCS-wide regulatory education and quality management programs pertaining to human subjects research and animal research;
  - Evaluates the institution's adherence to applicable federal regulations, state laws and accreditation standards, which govern human research;
  - Monitors changes in VA and other federal regulations, policies, manuals and handbooks;
  - Suggests systemic improvements in the institution's human research efforts that will either increase human subject safety or improve compliance with applicable federal regulations, state laws and accreditation standards, which govern human research;
  - Formulates institutional policies regarding protection of human and animal research subjects and laboratory personnel safety;
  - Works closely with other departments and entities including Biosafety, Radiation Safety, Environmental Health & Safety, Information Security Office, Privacy Office, Infection Control, Nursing Service, Performance Improvement, and the IRB to develop formal procedures for assuring appropriate flow of information necessary for a comprehensive institutional human subjects protections program;
  - Evaluates the outcome of the institution's changes that impact the conduct of human research and provide information to the R&DC and the ACOS/R&D as to whether these changes have led to improvements;
  - Conducts training, education and development of individuals responsible for the oversight or conduct of human research;
  - Disseminates information about research policies and procedures to the VAMHCS research community;
  - Responds to subject or staff complaints;
  - Prepares accreditations and reports;
  - Conducts the Participant Outreach program.
7. The Research Compliance Officer (RCO) reports to the MCD. The RCO is responsible for:
- Conducting the mandatory regulatory and informed consent audits of VAMHCS research protocols as required by VHA Handbook 1058.01: (1) conducting annual consent document audits, and (2) conducting triennial regulatory audits on all research protocols;
  - Informing the facility Director and research review committees about compliance concerns;
  - Administering the Office of Research Compliance (ORC) including its staff of Research Compliance Specialists and others;
  - Working collaboratively with the R&D Service to share information about compliance issues and to assist in program improvement;
  - Related duties as determined by the facility Director;
  - Is a non-voting consultant to the R&DC and its subcommittees.

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8. The Research Compliance Specialists in the ORC are responsible for:
- Conducting regulatory and informed consent, audits and other audits as assigned by the RCO;
  - Acting in the capacity of Research Compliance Officer when the RCO is absent.
9. The R&DC (R&DC)<sup>12</sup> is responsible through the COS, to the MCD for maintaining high standards throughout the facility's R&D Program. The R&DC reviews and approves all research activities prior to implementation at the VAMHCS. These standards include those assuring the scientific quality of the R&D projects, human subject rights, safety of personnel engaged in research, and welfare of animal subject, security of VA data, security of VHA research laboratories. It advises the Director on oversight, planning and execution of the R&D Program. All R&D activities within the facility, whether funded or unfunded, are within its purview. Other responsibilities include:
- Assuring the continuing high quality of the facility's R&D program;
  - Planning/developing broad objectives of the R&D program so that it supports the patient care mission of the facility;
  - Determining the extent to which the R&D program has met its objectives;
  - Overseeing all research activities for each VA facility for which it serves as the R&D Committee of record;
  - Reviewing all written agreements that establish: (a) A committee from another VA or non-VA entity in lieu of a required committee or subcommittee for the R&D Committee;
  - Reviewing and evaluating all R&D subcommittees both within the VA facility and at external entities that function in lieu of R&D subcommittees, such as affiliate Institutional Review Boards (IRBs), Institutional Animal Care and Use Committee (IACUC), or biosafety committees. A summary of these reviews and evaluations must be sent to the medical center Director annually;
  - Reviewing quality assurance activities, reports to the committee by the ACOS for R&D, AO for R&D, or other research staff members, subcommittee reports, facility reports or activities, and other appropriate sources;
  - Making appropriate recommendations to the medical center Director, including the suspension of a research study or remedial or restrictive action regarding a principal investigator;
  - Reviewing any apparent systemic deficiency that has a reasonable likelihood of substantially compromising the facility's research protection programs, including persistent failure by any subcommittee of the R&D Committee to adhere to the requirements governing VA research at its earliest practicable convened meeting, not to exceed 30 business days after the date of notification. (May hold unscheduled meetings in response to emergent issues in accordance with VHA Handbook 1200.01.)
  - Determining whether the notification involves an actual systemic deficiency

<sup>12</sup> See "R&D Committee" (HRP 01.03) and related PMs

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- that could substantially compromise the VA facility’s research protection programs, and if so: (a) determining what remedial actions, if any, are warranted to ensure effective research protections; and (b) notifying the VA facility Director and the ACOS/R&D within 5 business days after the determination.
- Evaluating research proposals for their relevance to Veterans’ health and to the missions of the VA and the VAMHCS;
  - Recommending, on the basis of such evaluations (type and quality of the research projects and effectiveness and needs of the HRPP) and after consideration of other needs, the distribution of R&D funds, space, personnel, equipment and supplies, and use of animal facilities both inside and outside the facility;
  - Reviewing and approving the R&D budgetary requests of the facility;
  - Recommending policies for the recruitment and development of personnel supported by R&D funds;
  - Evaluating the reports and approving the actions its subcommittees;
  - Reviewing and evaluating reports and results of compliance assessments and quality improvement activities related to research;
  - Reviewing and evaluating reports of complaints, allegations of research noncompliance or improprieties;
  - Implementing changes in regulations and policies relating to research, as directed by the ACOS/R&D;
  - Fulfilling such other functions as may be specified by the MCD;
  - Fulfilling VA requirements for the protection of research participants’ personal information and of research data security through the appointment of and advisement by the VAMHCS PO and ISO as non-voting members of the R&DC;
  - Following the principles, objectives, and functions outlined in VHA Handbook 1200.01, the R&DC will establish subcommittees on Human Studies [IRB], Animal Studies [IACUC], Space and Research Equipment, and Research Safety. These subcommittees will advise the R&DC on matters relating to each subcommittee. No research may be undertaken without R&DC and appropriate subcommittee(s) review and approval.
  - The ethical conduct of research and for human and animal subjects research protection.
10. The University of Maryland Institutional Review Board, is a VAMHCS IRB of record and is administered by the UM Human Research Protections Office (HRPO). It is responsible for the ethical review of research and the protection of human subjects. The VAMHCS accepts and follows the IRB’s SOPs when they are not superseded by VA SOPs. The IRB has agreed to follow VAMHCS requirements as outlined in the MOU.
11. The VA Central IRB (CIRB) is a VAMHCS IRB of record. It is responsible for the ethical review of VA Cooperative Studies Program (CSP) research projects. The

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VAMHCS accepts and follows the CIRB's SOPs. The CIRB has agreed to follow VAMHCS requirements as outlined in the MOU.

12. Investigators are ultimately responsible for their research protocols, the protection of the subjects enrolled in them, and the quality and actions of their research team members. Specific roles are listed in VHA Handbook 1200.05 §29. Some specific roles include:

- To be properly trained and to work within their scope of practice;
- To follow the research protocol as approved by the IRB and R&DC;
- To disclose conflicts of interest;
- To follow proper informed consent procedures, including HIPAA authorization;
- To report unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01.
- To maintain research records in accordance with RCS 10-1 and information security requirements;
- To ensure continued approval of the protocol by applicable oversight committees, without lapses in approvals;
- To ensure that they and their staff are knowledgeable about and follow all applicable VAMHCS and IRB SOPs, policies and procedures;
- To place participant rights and safety above all other aspects of their research endeavors;
- To ensure that they and their staff follow GCPs and federal regulations at all times;
- To be knowledgeable of and guided by the ethical principles described in Section II.A and the Belmont Report.

13. Research staff are responsible for the protection of the subjects enrolled in their protocols. Some specific roles include:

- implementation of protocols as approved by the IRB and R&DC;
- following proper informed consent procedures;
- becoming knowledgeable about and following all applicable VAMHCS and IRB SOPs, policies and procedures;
- following GCPs and federal regulations at all times;
- being knowledgeable of and guided by the ethical principles described in Section II.A and the Belmont Report.

14. Investigational Drug Service (IDS) and other Pharmacy Staff are responsible for adhering to policies and procedures for the receipt, storage, preparation,

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documentation and dispensing of investigational drugs (VHA Handbook 1108.4; VAMHCS SOP 119-010; R&D Service SOP HRP 05.01).

15. Privacy Officer (PO)<sup>13</sup> is responsible for oversight of facility policies consistent with national privacy policies including the Health Insurance Portability and Accountability Act (HIPAA), the VA Privacy Rule and VHA Handbook 1605.1. The PO is aware of special challenges related to privacy issues and the conduct of research. Some specific roles include:

- Developing VAMHCS privacy policies;
- Monitoring compliance with VAMHCS privacy policies;
- Reviewing or auditing all programs at the facility on a periodic basis to determine which programs collect, use, maintain and store individually identifiable information (III) in order to ensure compliance with VAMHCS privacy policies;
- Reporting all actual or suspected breaches of privacy of all III;
- Providing expert guidance to the VAMHCS on all privacy related matters such as the Privacy Act (PA), Freedom of Information Act (FOIA), HIPAA Privacy Rule and 38USC;
- Sitting on the R&DC as a non-voting member;
- Reviewing all human research protocols for privacy criteria as a requirement for R&DC approval;
- Raising privacy issues directly to the R&DC;
- Evaluating the effectiveness of documentation of Notification of Privacy Practices (NOPP) for non-veteran participants;
- Evaluating the effectiveness of documentation of accounting of disclosures of research participants' individually identifiable information (III).

16. Information Safety Officer (ISO)<sup>14</sup> is responsible for oversight of facility policies consistent with VA information security including VHA Handbook 6500. The ISO is aware of special challenges related to information technology (IT) issues and the conduct of research. Some specific roles include:

- Developing VAMHCS IT policies;
- Makes decisions on VA-sensitive and VA-protected information;
- Monitoring compliance with VAMHCS IT policies;
- Reviewing or auditing all programs at the VAMHCS on a periodic basis to determine which programs collect, use, maintain and store III in order to ensure compliance with VAMHCS IT policies;
- Reporting all actual or suspected breaches of IT policies;
- Providing expert guidance to the VAMHCS on all IT related matters;
- Sitting on the R&DC as a non-voting member;
- Reviewing all human research protocols for information security criteria as a requirement for R&DC approval (including Appendixes C and D);

<sup>13</sup> See "Review of Research Documentation for Compliance with Privacy Requirements" (HRP 01.12)

<sup>14</sup> See "Information Security Review of Research Protocols" (HRP 01.13)

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- Raising IT issues directly to the R&DC;
  - Ensuring that data is maintained on VA servers;
  - Ensuring that data are used only as specified in an approved protocol;
  - Ensuring that reasonable and appropriate protections are implemented;
  - Ensuring that data is appropriately protected before it is removed from the VA;
  - Ensuring that there is appropriate written authorization before data is removed from the VA;
  - Ensuring that IT equipment and storage devices are configured according to VA requirements.
17. The Executive Committee of the Medical Staff (ECMS), an arm of the Office of the Chief of Staff, reviews quarterly and annual reports on research compliance activities, presented by the ACOS/R&D and the Research Compliance Officer. This is an additional mechanism whereby senior Medical Center management maintains oversight of the HRPP.
18. The Patient Safety/Risk Management Program and Specialty Team Advising Research (STAR) provide the Research & Development Service with information, notification of problems (such as complaints, violations of policy, allegations of noncompliance), and guidance toward proper remediation.

## **V. Quality Management of the HRPP: Overview**

### **A. Policy**

The VAMHCS Research & Development (R&D) Service implements an integrated quality management program (QMP) as a component of the Human Research Protections Program, outlined in a written plan that encompasses privacy, information security, approval and conduct of a protocol, compliance with regulations, reportable events, investigational drug & device management, training & education of researchers, and oversight of the QMP (see sections VI-X). This program is a dynamic process and is subject to triennial review. Interim modifications to the plan may be made as warranted by regulatory changes and program needs.

### **B. Purpose**

- To monitor the implementation of the HRPP and to institute programmatic changes as necessary
- To establish a defined plan for the conduct and operation of a comprehensive and integrated QMP
- To support the mission and philosophy of the R&D Service (see Section I)
- To support the function of the R&DC and its subcommittees
- To comply with the requirements of external accrediting agencies as applicable

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- To provide evidence of a structured and effective quality management program

### **C. Structure**

The VAMHCS QMP establishes quality control and performance review processes that will incorporate but not be limited to the establishment of or access to:

- Tracking processes and databases with the capacity to identify the site and investigator for each research project and members of the research team (CICERO, ePROMISE);
- Tracking processes/databases with the capacity to track investigators', research team members and subcommittee members' mandatory human subjects protections trainings;
- Tracking processes /databases with the capacity to track research team qualifications such as documented research scopes of practice, completion of required trainings, and VAMHCS status (employee/WOC). As applicable, some staff will be subject to VA credentialing and privileging processes;
- A protocol review process to evaluate investigator compliance to the research protocol and, as applicable, clinical privileges, research scope of practice, and/or defined limitations for each investigator and/or allied research staff related to protocol implementation;
- A review process to evaluate investigator compliance with informed consent procedures and documentation (ORC audits);
- An auditing process directed to assessing the quality of regulatory compliance and protocol implementation by the investigators and other allied research staff (ORC audits);
- A review process for the use, storage, handling and dispensing of study agents, or agents used in research, following VAMHCS policies and procedures. Collaboration with the VAMHCS Pharmacy Service is essential;
- A review process to evaluate the effectiveness of research policies and procedures.

## **VI Quality Management Program: Privacy and Data Security<sup>15</sup>**

### **A. Privacy Requirements**

The VA has codified its enforcement of the Health Insurance Portability and Accountability Act (HIPAA) through its VA Privacy Rule and VHA Handbook 1605.1. The conduct of research within HIPAA requirements presents special challenges. The UM (through the IRB), the CIRB, and the VAMHCS (through the R&DC review process) evaluate the privacy risks of research proposals and must approve HIPAA documents and privacy protection plans according to established policies and procedures. The IRBs may approve waivers of HIPAA authorizations in accordance with regulations.

<sup>15</sup> References and applicable policy memoranda are located in Section XII.

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In compliance with VA mandates, the VAMHCS has named Privacy Officers who are non-voting members of the R&DC. A PO reviews each research proposal prior to IRB review to determine what health or individually-identifiable information (III) will be accessed, used or disclosed for the research study, the risks of (if any) and safeguards for disclosures of PHI and III, the adequacy of HIPAA authorizations or requests for waivers, and other required elements. All human research protocols must undergo PO review in order to be approved by the IRB and R&DC. The R&DC seeks the PO's guidance on privacy matters.

The ORC routinely evaluates the content and execution of HIPAA forms during the conduct of research studies and has the authority to evaluate investigators' compliance with their stated privacy plans.

The PO also evaluates the effectiveness of processes for documentation of Notice of Privacy Protections (NOPP) for non-veteran research participants (through VA Form 10-0483) and accounting of disclosures of research participants' information.

## **B. Data Security Requirements**

The VA has established rules for protection of data used in and derived from research projects. These rules apply to already existing data (retrieved for the purposes of the research), data created through the research, data repositories, and other uses of and transfer of VA research data.

In compliance with VA mandates, the VAMHCS has named Information Security Officers who are non-voting members of the R&DC. An ISO reviews each research proposal prior to IRB review to determine what types of data will be involved in the research project, where and how the data will be stored or transferred, the risks of security breaches, and other required elements. All human research protocols must undergo ISO review in order to be approved by the R&DC. The R&DC seeks the ISO's guidance on information technology (IT) matters.

The ORC has the authority to evaluate investigators' compliance with their stated IT security plans.

## **VII. Quality Management Program: Compliance and Quality Assurance of the Human Research Activities of Investigators (Auditing Program)<sup>16</sup>**

### **A. Approval of a Protocol**

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<sup>16</sup> References and applicable policy memoranda are located in Section XIII.

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The VAMHCS Quality Management Program begins with the protocol submission process. A summary of specific steps in the approval process is illustrated in Attachment 3.

In order for a human subjects protocol to be approved, a VAMHCS investigator must submit research projects to a VAMHCS affiliated IRB (University of Maryland IRB or the VA CIRB) and to the VAMHCS R&DC and its applicable subcommittees, all of which incorporate mechanisms for approving only those protocols that have scientific merit, that have resources available to conduct the research, and that can be conducted without undue burden or risk for participants. VAMHCS R&DC members and IRB members are required to have training in human research protections.

No VAMHCS human research can begin until approvals of the R&DC and applicable subcommittees have been obtained and until the ACOS/R&D has notified the investigator that the research can be initiated. The IRB is responsible for decisions on human subjects research, exempt status, expedited review, investigator conflict of interest and its management, the validity of IND and IDE numbers or decisions about IND and IDE exemptions.

VAMHCS R&D Service has provided guidance and tools for its “Collaborative Studies Program”, an evolving program based on guidance from VHA Office of Research Oversight issued in 2011. This program is intended to clarify research protocols that are conducted at both the VAMHCS and at the University of Maryland or other collaborators with regard to disclosure of VA research data to academic affiliates and other non-VA entities, records retention, data ownership, and data security. It does so by requiring delineation of research activities that occur at each location: recruitment, consent, research activities, data storage and transfer, access of databases, use of resources (staff paid time, equipment, services, etc.). The R&DC approves the VA portions of the delineated protocol. The VAMHCS collaborative studies program is currently undergoing extensive review and improvements.

Tools and checklists to assist research staff with writing and submitting protocols and informed consent documents are available through the R&D Service and IRB websites. Research staff must ensure that all portions of the research application are complete and consistent with each other: informed consent form, HIPAA authorization, research protocol, CICERO application, collaborative studies tools, etc.

Both the IRB and the R&DC require that Department Chairs or their designees to review new protocols for scientific merit, feasibility and resources available for the work, and investigator qualifications, and sign-off on them before they are submitted to the committees.

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As part of their determination of whether a protocol fulfills the regulatory criteria for approval, the IRB considers the scientific merit of the project,<sup>17</sup> the quality of the informed consent document, and the balance between risks and benefits for subjects. The CICERO (Comprehensive Institutional Collaborative Evaluation of Research On-line) system, a paperless protocol submission process which went on-line on the UM/VAMHCS research campus in 2008, prompts investigators to populate information into the “CICERO application” and to submit informed consent and HIPAA documents using available templates, and a completed “Checklist for Reviewing Privacy, Confidentiality and Information Security in Research-New Submission”. The CICERO submission is electronically approved by the investigator’s department head(s) (who certify that they have reviewed it for scientific merit and feasibility) before it is then passed on to IRB analysts and other applicable reviews. As part of the IRB’s review of the submitted protocol, the ISO and PO submit their reviews through their comments on the “Checklist for Reviewing Privacy, Confidentiality and Information Security in Research-New Submission.” If applicable, the protocol is also reviewed by the Radiation Safety Committee.

The R&DC, through its administrative reviews and the recommendations from its subcommittees, considers the scientific merit of the proposal, the logistics and funding for the project, the expertise and qualifications of the investigator and team members, the quality of the informed consent document, and the balance between risks and benefits for subjects<sup>18</sup>. If applicable, protocols are also reviewed by the Investigational Drug Pharmacist as part of the R&D submission process. The R&DC also assesses the utilization of VA resources. It will not approve a project unless the protocol, ICF, DSMP and HIPAA authorization/waiver have received IRB approval and unless principal investigators have proper levels of credentialing and training. There are a flowchart and checklists available to investigators and committee members to assist them in this process.

Investigators are required to complete OGE Form 450 Alternative-VA at the time of R&DC initial submissions and annual reviews. Until VA ORD provides information and training on evaluation of COI, the VAMHCS RCOIO consults with the R&DC and Regional Counsel as necessary. Procedures for evaluating and managing COI in these instances are discussed in HRP 01.17 “Conflict of Interest.” Procedures for evaluation and management of institutional COI and individual financial COI are discussed in IRB policies and procedures and in R&D Service SOP, HRP 01.17.

Chairs and members of the R&DC and subcommittees who have a conflict of interest are prohibited from R&DC votes on issues in which they have the conflict. The Chair, committee member(s), or senior administrative staff with a conflict of interest will verbally disclose the conflict of interest to the R&DC Chair or Co-chair or subcommittee

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<sup>17</sup> IRB P&P

<sup>18</sup> HRP 01.03 “Research & Development Committee”

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Chair or Co-chair and will recuse themselves from any discussion and voting on such research except when asked to answer questions from the R&DC or subcommittee. The Research COI Officer may also request or require that a member recuse himself/herself from deliberations. Recusals will be noted in the minutes of the R&DC or subcommittee meeting.

Chairs and members of the R&DC and its subcommittees should be free of undue influence from others. If committee or subcommittee members have concerns about undue influence, they should contact the VAMHCS RCO, the ACOS/R&D, the VAMHCS R&DC Chair, or the MCD. [HRP 01.03]

The Investigational Drug Pharmacist (IDP) is a permanent member of the VAMHCS R&DC, and her input is an essential element of the R&D review and approval process. The custody and dispensing of drugs involved in approved protocols occur through the Investigational Drug Service except for projects where the drug intervention occur at the University and are controlled through the UMMS investigational drug service. If the University dispenses study drug(s), there must be a written plan that is approved by the VAMHCS IDP and the VAMHCS Chief, Pharmacy Services (VAMHCS SOP 119-010).

During the course of a study, it is often necessary to amend the protocol, the informed consent form, the logistical details provided in the CICERO submission, or other aspects of the study. In this case, investigators must submit a “Modification Request” to the IRB. The IRB reviews and approves modifications in a process similar to that described for initial submission. The investigator/staff submits the IRB-approved modification to the R&DC for review.

As part of the IRB submission, the CICERO system triggers the PI to submit a DSMP. The PI must submit an acceptable DSMP at a level of safety monitoring appropriate to the protocol in order for the protocol to be approved. The Research Compliance Officer and Research Compliance Specialists have “read-only” access to CICERO for VAMHCS protocols in order to examine DSMP reports and reportable events. Further details on DSMPs on campus and on reportable events are found in the relevant IRB P&P.

## **B. Conduct of a Protocol: Study Lifecycle**

Recruitment of participants may not begin at the VAMHCS until the protocol has been approved by the IRB and VAMHCS R&DC. In the CICERO application, Investigators provide a detailed description of the recruitment methods and materials which must then be approved by the IRB. VAMHCS studies will employ IRB- and R&DC-approved VAMHCS research informed consent forms and recruitment letters. VA recruitment may not occur through a “cold call process” (an R&DC-approved recruitment letter must precede any phone calls), and social security numbers may not be requested over the phone. In subsequent calls, the research team re-introduce themselves to the participant by referring to previous contacts and, when applicable, the information provided in the informed

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consent form, and ensuring that the scope of telephone contacts with the subject is limited to topics outlined in IRB-approved protocols and informed consent forms.

In general, a participant may not be screened for a study until a process of informed consent has concluded with a signed informed consent form unless the IRB has approved a waiver of informed consent, a waiver or alteration of documentation of informed consent, and/or a HIPAA waiver<sup>19</sup>. The PI may formally delegate qualified staff (in writing) to perform the informed consent process<sup>20</sup>. The PI must provide a detailed description of the informed consent process in the CICERO protocol. Under certain circumstances, the IRB may grant a waiver of written informed consent (see IRB P&P and VAMHCS HRP 03.01G).

When subject recruitment/enrollment begins, research enrollment notes must be entered into CPRS *only when research procedures or interventions are used that may impact the medical care of the research subject*. This applies to participants who are VAMHCS inpatients (whether or not the admission was for research purpose), VAMHCS outpatients or others (if the research intervention or procedure occurs at VAMHCS medical facilities, VAMHCS Annex, etc.). Even if a CPRS chart exists for the participant, there is no requirement to enter enrollment notes unless the research intervention may impact the medical care of the research subject. Additional research progress/procedure notes must be entered into CPRS if the research intervention may impact the medical care of the research subject or if the principal investigator, medical advisor, or clinical research team members determine that a CPRS note is advisable with regard to the medical care of the participant. In addition, a “Research Subject Clinical Warning” must be placed in the subject’s electronic medical chart (CPRS) if the study involves the use of an investigational drug or investigational device. Investigators may choose to use an RSCW for other reasons if it will contribute to the safety of research participants or will assist in the conduct of the study. The IRB may choose to require an RSCW for participant safety or other issues.

The investigator must maintain a master list of all subjects from whom informed consent has been obtained whether or not the IRB granted a waiver of documentation of informed consent (see 38 CFR 16.117(c) and par. 34). Investigators must not add a subject’s name to the master list of all subjects until after: informed consent has been obtained from that subject, and, when appropriate, informed consent has been documented using an IRB-

<sup>19</sup> Studies that are granted a HIPAA full waiver or a waiver for recruitment purposes, *by the IRB*, may screen patients prior to obtaining informed consent.

<sup>20</sup> If the PI or LSI does not personally obtain informed consent, the investigator must formally and prospectively designate to another research team member in writing the protocol or the application for IRB approval the responsibility for obtaining informed consent, whether or not a waiver of documentation of informed consent has been approved by the IRB. This designee must be a member of the research team and must have completed required human research protections, GCP and VHA trainings and be knowledgeable enough about the protocol to answer the questions of prospective subjects; must be acting within their research scope of practice; and must have a VA appointment/employment and be properly credentialed. [1200.05 9,j(1)]

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approved informed consent form. The investigator must secure the master list in the investigator's file for each study in compliance with all VA confidentiality and information security requirements.

The "Research Subject Clinical Warning" flags when the patient's electronic chart is opened, making clinicians immediately aware of important information on the drug/device and study as well as contact information for study staff. Details are found in the SOP "Enrollment Notes for Research Participants" (HRP 07.01).

All research participants, whether veterans or nonveterans, must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA medical facilities as in-patients, treated as outpatients at VA medical facilities, or when research procedures or interventions are used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or nursing homes) (see VHA Handbook 1907.01). Informed consent documents are not required to be in the health record. A record must be created when the research requires use of any clinical resources, such as: radiology, cardiology (e.g., electrocardiogram, stress test, etc.), clinical laboratory, and pharmacy; or if there is a reasonable chance that the research intervention may lead to physical or psychological AEs. This allows research progress notes to be recorded (if applicable), and laboratory tests, imaging studies, etc. to be performed and reported. It also allows the participant to be pre-registered in the VA system if there is a reasonable risk for adverse events. Research enrollment notes must be entered into CPRS only when research procedures or interventions are used that may impact the medical care of the research subject. (See HRP 07.08 for details)

As participants complete their study participation, research staff enters study completion notes in CPRS/the study record and ensure that RSCWs are removed from CPRS (if applicable).

Data collection, record keeping and organization are expected to meet high standards during all phases of study conduct. Concerns for participant safety and rights are expected to take top priority in decisions made by investigators and staff. During the course of the study, investigators/staff are required to report serious local unexpected and related adverse events, unanticipated problems involving risks to subjects (UPR) or others, self-identified potential noncompliance, any audit reports or other reports of internal or external monitoring activities, and other reportable events to the IRB via CICERO according to the "Reportable New Information" (RNI) process. Any proposed changes to a research study in response to an unanticipated problem or reportable event must be reviewed and approved by the IRB before being implemented, except when necessary to eliminate apparent immediate hazards to subjects. The IRB reviews reportable events and reports its findings in accordance with VHA Handbook 1058.01.

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Investigators may choose to ‘close studies to enrollment’ at the IRB and may thereby qualify to reduce the risk level determination while participant follow-up and/or data analysis continue. Investigators may close their studies at the IRB once all interactions with participants or their identifiable data has been completed. Protocols must remain open at the R&DC until data analysis is completed, whether the data is deidentified or not.

Once data analysis is complete and all study-related activities have ended, the investigator must notify the IRB (through CICERO), the R&DC (through the R&DC coordinator) and the Chief, Pharmacy Services (through the Investigational Drug Pharmacist) (if applicable). The Office of Research Compliance must audit studies at the time of closure or within the audit year of the closure.

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**C. Conduct of a Research Project: Oversight**

Once a study is actively enrolling participants, the day-to-day operations of the Investigators and their staff are subject to periodic assessment. Such assessments indicate the extent to which the Investigators comply with VA and Federal regulations and the adequacy of their research processes and documentation. Assessments may include chart audits as well as interviews with investigators and staff and observations of informed consent discussions with prospective participants. Investigators and staff have several VAMHCS resources at their disposal (through the R&D Service website) to guide them through the recruitment, informed consent and study documentation phases (“Informed Consent Guidebook” (HRP03.01G), “Guidelines for Setting up a Study Binder and Regulatory Documents Binder” (HRP 07.02G), “Guidance on Source Documents” (HRP 07.03G)).

The ORC annually conducts audits of signed informed consent forms and conducts regulatory audits at least every three years for studies initiated after 1/1/2008 and any currently open studies that initiated prior to 1/1/2008. The ORC conducts for-cause or other audits at the request of the IRB or the MCD. The ORC must also conduct audits at the time of study closure or within the audit year of the closure. All ORC audits are conducted and reported in accordance with VHA Handbook 1058.01 and ORO guidance. Investigators are required to notify the R&D Service when they host external monitors for site visits. All active VAMHCS protocols are eligible for audit, regardless of funding source. Audits are generally driven by the ORO mandatory audit program, but for-cause audits may also be conducted. Audits are conducted according to the ORC’s internal procedures and audit plan.

**1. Consent Process**

The ethical conduct of human research is based upon the voluntary consent of the subject who has been appropriately informed about a study’s risks and benefits. It is the responsibility of the investigator to ensure that all federal and state regulations have been met through the language of the informed consent document, and that informed consent itself has been properly obtained from the subject or the subject’s legal representative. Documentation of the informed consent process is required to establish that the subject was accurately and adequately informed, that they exhibited understanding of the study, that they had a chance to ask questions, that they received a copy of the signed documents, and that no study-related procedures were initiated prior to obtaining informed consent. The process also includes obtaining HIPAA authorization.

The R&D Service promotes these investigator obligations by providing instructional manuals and sample tools such as guidelines on informed consent, source documentation, and regulatory documents (see list in Section XI). It also offers opportunities to personally consult with the HARPO and other resources. The Informed Consent

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Guidebook (HRP 03.01G) is highly beneficial in guiding investigators and research staff through this process.

Special circumstances regarding vulnerable populations and persons with impaired decision making capacity (IDMC) are described in HRP 03.03 “Obtaining and Documenting Informed Consent”, the Informed Consent Guidebook (HRP 03.01G) and IRB P&P and are consistent with VHA Handbook 1200.05.

Both the ORC and the IRB have the authority to observe the consent process between an investigator/research staff and a prospective subject and to make judgments as to its effectiveness and compliance with institutional standards.

Based on the audit reports prepared by the ORC, the ORC evaluates the effectiveness of the process for documentation of consent. This evaluation includes documentation that procedures such as the following have been conducted:

- Consent has been obtained prior to initiating any research related procedures.
- Only the IRB-approved consent form has been used.
- The consent document has been signed and dated by the subject (or the subject’s legally authorized representative) and the individual providing the information to the subject.
- The consent document includes research-related injury language and, if FDA regulated, contains a statement on [clinicaltrials.gov](http://clinicaltrials.gov).
- The subject’s research and/or medical records (CPRS) document the consent process with an appropriate note and original, signed consent document.
- There is documentation that the subject or the subject’s legally authorized representative was provided a copy of the consent document.
- Evidence that the subject has been properly informed of his/her privacy rights and that a HIPAA authorization form has been signed if applicable.

## 2. Compliance with Regulations, Policies and Guidelines

The principal investigator (PI) is the individual of record who assumes the authority and responsibility for the conduct of a clinical study according to all applicable VHA, IRB, and other local and federal requirements. By signing Form FDA 1572, the PI agrees to comply with the conditions required by the FDA for use of investigational articles. By signing an assurance (FWA) with OHRP, the Institution agrees to comply with the conditions required by that Agency for the conduct of human research. In order to accept VA funding or conduct research at the VAMHCS, the PI must agree to comply with the Common Rule as set forth in 38 CFR 16. The PI has the authority to delegate responsibility to individual members of the research team; however, the PI is ultimately responsible for the overall conduct of the study.

As long as the human research is conducted by a VA investigator, on VA property, or with VA resources or data, adherence to the federal regulations, VHA Directives and

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Handbooks, VAMHCS policies and IRB SOPs is required. If during routine QA/QI activities, a PI is found to be noncompliant with the federal regulations or institutional policies that govern human research, the non-compliance will be reported to the R&D Service for further action. QA/QI and other operations activities that could be research are addressed in VHA handbook 1058.05. Local VAMHCS policy on this matter is currently undergoing concurrence.

Non-compliance may come to light as a result of routine audits, for-cause audits, or complaints or allegations from participants or staff. The Research Compliance Officer proceeds according to VHA Handbook 1058.01 and local VAMHCS procedures for noncompliance found through audits. As applicable, the IRB, the VAMHCS R&DC, ACOS/R&D, COS, MCD, VISN ORO regional office and VHA Central Office are apprised of allegations and findings.

The VA R&DC, through the COS or MCD and with notification to the HRPO Director of Quality Improvement, may recommend that the MCD suspend or terminate the research at the VAMHCS. The IRB may take further actions based on its policies and procedures. The R&DC may implement other measures to safeguard research subjects over and above the HRPO's corrective action plan (CAP); however, it may not negate or lessen any parts of the HRPO CAP. These additional measures could necessitate amendments to the protocol at the IRB

### 3. Study Conduct

During the recruitment phase of a human research study, the Investigator and the research team are expected to follow the approved recruiting procedures. After potential subjects have been identified through recruitment efforts, the process of subject selection begins. It is imperative that subject selection is in accordance with the inclusion/exclusion criteria to ensure maximal subject safety during the trial. Once enrolled, the safety and well-being of subjects should be of paramount continuing concern to the research team. Through close monitoring and careful assessment of subjects, adverse events can be detected early and treated appropriately. By following the protocol, close attention is paid to subject well-being and to integrity of the data.

The ORC evaluates research study activities for compliance with applicable regulatory requirements. This evaluation may include assessments of the following criteria:

- Regulatory documentation (protocol submissions, approvals, modifications, continuing reviews) related to the IRB, R&DC, and other applicable subcommittees
- Obtaining IRB approval prior to initiating changes to the protocol or consent form, except where necessary to eliminate apparent immediate hazards to subjects
- Documentation of inclusion/exclusion criteria
- Adherence to IRB approved protocols and conditions
- Reporting of applicable unanticipated problems involving risks to human subjects or others, serious adverse events, and safety reports

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- Staff qualifications and applicable education and training
- Credentialing and research scope of practice of applicable staff.

#### 4. Unanticipated Problems, Unanticipated SAEs and DSMP Conduct and Reports

The R&D Service requires investigators to report serious, local adverse events and unanticipated problems involving risks to participants or others according to UMB IRB and VA CIRB P&P. Reporting to UMB IRB is done via CICERO as soon as possible but within 5 working days of the investigator becoming aware of the problem. CICERO sends automatic notifications to the VAMHCS HARPO when a report on a VAMHCS study has been filed.

The VA defines “unanticipated (unexpected)”, “adverse event”, “serious adverse event (SAE)” and “serious problem” as follows:

- Adverse event (AE) for VAMHCS Research: Any untoward occurrence (physical, psychological) in a human subject participating in research.
- Unanticipated (unexpected): The terms “unanticipated” and “unexpected” refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.
- Serious adverse event (SAE): An SAE is an AE in human research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome.
- Serious problem: A serious problem is a problem in human research that may reasonably be regarded as: (1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or (2) Substantively compromising the effectiveness of a facility’s human research protection or human research oversight programs.

At the UM HRPO, reports of serious local unanticipated problems or local unanticipated SAEs are initially reviewed by a qualified IRB member-reviewer to determine whether any actions are warranted to eliminate apparent immediate hazards to subjects. The IRB notifies the VAMHCS MCD and ACOS/R&D in writing, in accordance with VHA Handbook 1058.01 §7.d(3). The MCD notifies ORO within 5 business days of receiving the IRB’s notifications.

Through CICERO access and attendance at IRB meetings, the VAMHCS HARPO can review each report of VAMHCS-related unanticipated problems and takes action as indicated by the circumstances of the event. This includes reporting the event/problem to the R&DC, the ACOS/R&D, the COS, the MCD, the FDA, OHRP, ORO, ORD (for VA-funded studies), other VAMHCS officials, and patients as indicated by the circumstances of the event/problem and standard procedures. Reporting the unanticipated problem to

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ORO, VA Central Office and others is in accordance with ORO guidelines as outlined in VA Handbook 1058.01 The Investigator must report applicable adverse events/problems to the Sponsor/coordinating center according to the Sponsor's/coordinating center's procedures.

Following NIH and other guidelines, the VAMHCS and the University of Maryland HRPO have instituted DSMPs for all studies on the UM/VAMHCS campuses. At the time of protocol submission, Investigators are triggered by CICERO to submit a DSMP appropriate to the type of study and the risks associated with it. Investigators must also submit DSMB reports to the IRB at the time of continuing review. The structure of DSMPs is discussed in IRB P&P.

#### 5. Investigator Internal Policies and Standard Operating Procedures

Investigators are encouraged to establish standard operating procedures within their own research programs. By establishing their own internal SOPs, “study specific” SOPs (SSSOPS)<sup>21</sup>, standard forms, and consistent policies that are rooted in institutional and regulatory norms, Investigators engage in Good Clinical Practices, promote the safety of their research subjects and ensure scientific integrity of their projects.

Investigators are strongly encouraged to include mechanisms for auditing their own compliance with their SOPs, SSSOPs, or institutional policies and procedures. Investigators should conduct internal quality assurance according to R&D Service SOP “Investigator Internal Quality Assurance” (HRP 02.04).

The HARPO is available to assist Investigators to develop such programs. Both the HARPO and the UM Human Research Protection Office are available for consultation or mentoring and can provide checklists, self-assessment tools, templates for SOPs and forms, and other guidelines on their web sites or in person.

#### 6. Complaints<sup>22</sup>

Complaints and suggestions from participants, their families, research team members, the community or others are taken seriously and may generate inquiries or for-cause audits. The HARPO processes complaints according to HRP 01.07.

The primary mechanism for research participants and research personnel to address their complaints about a research project is through contact with the VAMHCS HARPO, but also the ORC or the UM IRB. The IRB-approved informed consent document includes

<sup>21</sup> SSSOP: Study-Specific SOP; a recommended practice to standardize the conduct of a specific study by the research group. See Research Service Guideline: “Study-Specific SOPs (SSSOPs)” (HRP 07.06G)

<sup>22</sup> See “Addressing and Responding to Comments, Complaints and Suggestions Related to the Human Research Protection Program” (HRP 01.07)

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the telephone contact information for the Principal Investigator, study staff the IRB, and the HARPO. ICFs for VAMHCS studies contain contact information for the VAMHCS investigator(s) involved with the protocol. The VAMHCS Research and Development website lists several phone numbers and e-mail addresses may be used by research subjects and the general public to contact the VAMHCS HARPO about their concerns.<sup>23</sup>

A complainant contacts the HARPO or the UM HRPO and has the choice of remaining anonymous or of providing identifying information that is necessary if they wish to be informed of the progress and results of the investigation.

If the HRPO receives a complaint that involves a veteran, a subject in a VA-approved study, research conducted on or with VA property, data or staff, the HRPO notifies the HARPO. The HARPO then proceeds according to VAMHCS R&D Service “Comments, Complaints and Suggestions Related to the Human Research Protection Program” (HRP 01.07). Possible actions are outlined in the SOP.

If a complaint appears to be indicative of possible noncompliance, the HARPO proceeds according to VHA Handbook 1058.01 and local procedures.

If a complaint is indicative of an “unanticipated problem involving risks to participants or others” or other reportable event, the HARPO instructs the investigator to submit a report to the IRB.

#### **D. Actions & Reports**

The ORC’s audits may result in any of the following actions:

- The ORC finds that an Investigator is in compliance with internal, institutional and regulatory requirements.
- The ORC finds general compliance with internal, institutional and regulatory requirements but finds that some action is required in order to be in full compliance.
- The RCO finds apparent serious or continuing noncompliance. The RCO notifies the IRB through submission of an RNI identifying the apparent serious and/or continuing noncompliance. If the IRB determines that serious and/or continuing noncompliance has occurred, the VAMHCS MCD and ACOS/R&D are notified. After a review of the situation, the MCD, the convened R&DC, the IRB chair, or the convened IRB will take or require appropriate corrective actions, which may include suspension of new enrollment, and study termination (see UM P&P and RCO local P&P).
- The ORC discovers systemic deficiencies within institutional policies and procedures. These deficiencies will be brought to the attention of the R&DC and ACOS for R&D. The R&DC proceeds according to VHA Handbook 1058.01 §5.i and local R&DC procedures. Special reporting to VHA Office of Research Oversight (ORO) may be

<sup>23</sup> [http://www.maryland.research.va.gov/contact\\_us.asp](http://www.maryland.research.va.gov/contact_us.asp)

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required [VHA Handbook 1058.01]. The COS or MCD may charter a root cause analysis of the problem and the root cause analysis team will formulate a corrective action plan. This corrective action plan may require new policies or procedures.

The Research Compliance Officer reports to VAMHCS entities according to the following table:

(Table 1: RCO reports)

<b>Person / Committee</b>	<b>Frequency</b>	<b>Content</b>
R&DC	Monthly	Issues, audit reports, audit activity, compliance cases
MCD	Monthly	Ongoing compliance issues, audits, staffing, strategies
VISN leadership	As requested	As requested
EPIC	Quarterly	QA reports
IRB	As needed	Presentation of cases of apparent noncompliance, follow-ups on cases determined to be serious or continuing noncompliance.

### **VIII. Quality Management Plan: Investigational Drug Service<sup>24</sup>**

The day-to-day operations of the Investigational Drug Service (IDS) are subject to periodic assessment. Such assessments will determine the extent to which the IDS complies with VA and Federal regulations, and the adequacy of its processes and documentation.

The effectiveness of the IDS' compliance depends in large part on Investigators' compliance with VAMHCS research policies and procedures as well as the IDS' own day-to-day operations. Therefore, it is necessary to have an integrated approach between the IDS, the HRP Program, and investigators.

The VAMHCS Investigational Drug Service Pharmacist (IDP) and the HARPO work closely together to develop complementary policies and procedures, to share information regarding possible non-compliance of investigators, to communicate regarding IRB status of protocols, to adjust standard operating procedures in response to regulatory changes, to perform root cause analysis of pharmacy-related problems or problems whose resolution may affect the Investigational Pharmacy, to develop resolution plans, and to comply with JCAHO and accreditation standards.

<sup>24</sup> References and applicable policy memoranda are located in Section XII: 13, 22, 23.

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The IDP sits on the VAMHCS R&DC where s/he can provide expertise on VA protocols as well as become aware of protocols that will or should require the use of IDS services. Because a number of VAMHCS studies entail the use of drugs, the IDP is uniquely situated as a gatekeeper to detect problems and monitor the effectiveness of corrective action plans.

At the time that investigators submit protocols for approval by the R&DC, they are required meet with the IDP in order to establish the terms of an “IDS Agreement”.

Study drugs are dispensed through the VAMHCS IDS except for projects where the drug interventions occur at the University and are controlled through the UMMS investigational drug service. If the University dispenses study drug(s), there must be a written plan that is approved by the VAMHCS IDP and the VAMHCS Chief, Pharmacy Services (VAMHCS SOP 119-010).

Plans for the control of study devices are approved by the UM IRB and VA R&DC. In most cases, study devices are managed by the investigators or their staffs. However the IDS may also be designated to manage investigational devices.

Before any study drug can be dispensed to a subject, the following must be on file in the Investigational Pharmacy or accessible by the IDS Pharmacist’s access to CICERO:

- A copy of the approved protocol
- A copy of the current, approved ICF
- IRB approval letter
- R&D approval letter
- Investigator’s brochure (if applicable)
- A completed VA form 10-9012
- A drug dispensing log(s)
- A record that the pharmacist has viewed a signed copy of each signed informed consent document or signature page.

Dispensing of study drug cannot take place unless an electronic order (entered into CPRS or VISTA by the investigator, designee or Investigational Pharmacist) or a paper prescription signed by the PI or designee is submitted to the IDS Pharmacist (designated personnel must be specifically listed on the 10-9012).

The IDS Pharmacist has CICERO access to VA studies in order to check on the current status of amendments or changes in informed consent forms.

Dispensing logs or documentation must contain the following elements:

- name of the study drug
- name of the manufacturer or drug source
- date of receipt of drug
- quantity received

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- expiration date or “retest date”
- control number or lot number
- date of IRB approval + date of R&D approval
- name of the authorized practitioner signing the study drug prescription/order (at the VAMHCS, this can be documented in CPRS)
- name of the patient or subject’s initials
- serial number of the prescription/order (at the VAMHCS, this can be documented in CPRS or VISTA)
- quantity of drug dispensed
- balance of study drug
- dispensing pharmacist’s initials
- disposition of unused drug.

The HARPO may conduct audits of the Investigational Pharmacy on a routine or for-cause basis. The audit includes:

- Presence (or access through CICERO) of approved protocol, approval letters, signed ICFs and 10-9012
- Records of storage and security of investigational drug supply
- Records of receipt and dispensing of investigational drug supply
- Investigational drug logs/records containing the following information: name of drug, manufacturer/source, date of receipt of drug, quantity received, expiration date, control number, date of protocol approval, name(s) of authorized practitioner signing prescription/CPRS order, serial number of prescription/CPRS order, quantity dispensed, balance after transaction
- Records/SOP/demonstration of disposition of unused stock

The procedures by which this is accomplished are described in detail in the following SOPs and audit tools:

- Investigational Drug Section, VAMHCS SOP No.119/010
- Auditing the Investigational Pharmacy (HRP 02.05)

The HARPO’s evaluation of the Investigational Pharmacy may result in any of the following actions:

- The HARPO finds that the Investigational Pharmacist is in compliance with internal, institutional and regulatory requirements for compliance and documentation.
- The HARPO finds general compliance with internal, institutional and regulatory requirements for compliance and documentation but finds that some action is required in order to be in full compliance. The HARPO works with the Investigational Pharmacist to develop corrective policies and procedures.
- The HARPO finds significant deficiencies in the Investigational Pharmacist’s compliance and documentation and immediately notifies the ACOS for Research. If necessary, VAMHCS stud(ies) are suspended until corrective actions are in effect.

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More detailed, for-cause audits and/or intensive consultations may be necessary in order to formulate remedial actions.

- The HARPO discovers systemic deficiencies within institutional policies and procedures.

### **IX. Quality Management Plan: Staff Qualifications, Education and Training**

No HRPP can be implemented unless investigators, research staff, and committee/subcommittee members are thoroughly educated about the HRPP and trained in its implementation. They must also have an understanding of the ethical and regulatory foundations of human research subject protections in order to promote adherence to principles, rules and regulations. This requires a multilevel approach:

1. Basic education and training required to fulfill position description/functional statement
2. Basic education about research ethics and human subject protection,
3. Specific knowledge about the VAMHCS HRPP/QMP, and
4. Continual or periodic updates on changes in the HRPP/QMP, VA regulations, federal and state regulations, UM IRB policies and procedures, and other institutional changes.

A summary of educational requirements is available in Table 2.

All VAMHCS employees, whether funded or “without compensation” (WOC), and who are engaged in research (see section II.B) must complete the education and training requirements listed below.<sup>25</sup> Employees and WOCs must also submit documentation of their Research Scope of Practice for their involvement in a protocol.

Investigators/supervisors establish Research Scopes of Practice (SoP) for their VAMHCS research team members (both licensed and unlicensed) and ensure that the team member is qualified and trained to perform the research tasks. SoP’s apply to the individual and may cover the individual’s activities on multiple research projects. SoP’s should be reviewed with the team members annually and updated as necessary. Initial SoP’s are signed by the ACOS/R&D and are subject to ACOS/R&D’s annual audit of SoP’s. In addition, all members of the R&DC and its applicable subcommittees must complete applicable education and training requirements.

The VAMHCS R&D Service accesses the Talent Management System (TMS) Collaborative Institutional Training Initiative (CITI) to confirm that individuals in the above categories (investigators, applicable research staff, committee and subcommittee members, etc.) have completed the VA training requirements and have a SoP signed by the ACOS/R&D in place.

<sup>25</sup> See SOPs 04.02 “Research Personnel Training”

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In general, all staff are responsible for maintaining their own training requirements/certifications, however PIs are responsible for ensuring that the trainings, research scopes of practice, credentialing, WOC/employment status of their co-investigators and team members are current. No protocol will be accepted for review by the VAMHCS R&DC if the investigator's and VAMHCS team members' VA training requirements are not up to date.

It is also recognized that QMP outcomes can serve to identify opportunities for staff education and knowledge/skills enhancements. It is imperative that research staff and, when appropriate, hospital-wide staff be informed of discoveries and actions developed through root-cause analysis of adverse incidents and audit results. Interaction with the committees previously listed can be an additional source for performance improvement and education.

1. Basic education and training required to fulfill position description/functional statement

All investigators and VAMHCS research team members must have appropriate education and training to qualify them for the positions that they fulfill and the activities that they perform for research purposes. VAMHCS investigators and research staff must provide documentation for the following requirements:

- a. Completion of appropriate level of basic education;
- b. Completion of appropriate level of professional training;
- c. Valid licensure, registrations and /or certifications and VA credentialing for all licensed research staff whose research activities fall under their license, registration or certification must be credentialed through the Department of Veterans Affairs (VA). (credentialing/VetPro).
- d. A Research Scope of Practice Statement that clearly defines the parameters or functions that are allowed or not allowed to be performed as part of the duties of the individual;

2. Basic education about research ethics and human subject protection

All investigators, research team members and members of oversight committees who are involved in human studies research will receive appropriate training in the ethical principles and accepted practices for conducting human studies research. VAMHCS investigators and research staff must provide documentation for the following requirements:

- a. Triennial human research protections training through the Collaborative Institutional Training Initiatives (CITI) at [www.citiprogram.org](http://www.citiprogram.org) (Staff may take the VA CITI curriculum or the UMB CITI curriculum.)
- b. Optional triennial Good Clinical Practices (GCP) training through CITI or its equivalent. [www.citiprogram.org](http://www.citiprogram.org).

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- c. Annual “VA Privacy Policy” Web training (HIPAA training specific to the VA). See the R&D Service training/education webpage<sup>26</sup> for current information on access.
- d. Annual “Privacy and Information Security Awareness and Rules of Behavior” (formerly “Cyber Security”) training. See the R&D Service training/education webpage for current information on access.

Additional information can be found in the R&D Service SOP “Research Personnel – Mandatory Trainings” (HRP 04.02).

2. Specific knowledge about and/or recent changes in campus research policies and procedures (VAMHCS HRPP/QMP, IRB SOPs, UMB policies & procedures) is communicated to VAMCS investigators and research staff by the Research Compliance Office through the following methods:
  - a. R&D Service website: [www.maryland.research.va.gov](http://www.maryland.research.va.gov).
  - b. Research Service Hot Topics series:  
[http://www.maryland.research.va.gov/hot\\_topics.asp](http://www.maryland.research.va.gov/hot_topics.asp)
  - c. Research Service “Brown Bag Lunch & Learns”
  - d. Email broadcasts to investigators and research staff
  - e. Investigator/staff education sessions
  - f. Education designed to improve adherence to the HRPP
  - g. Other mandatory or other Town Hall meetings
  - h. Manuals
  - i. HRPO education sessions
  - j. Individual/group trainings/consultations as requested
  
3. Updates on changes in other/external regulations, policies and procedures (ORD, ORO FDA, OHRP, other federal and state agencies)
  - a. Research Service Hot Topics series
  - b. Brown Bag Lunch & Learns
  - b. Email broadcasts to investigators and research staff
  - c. Individual/group trainings/consultations as requested
  - d. Continuing education activities offered by research-related professional organizations such PRIM&R, ACRP, DIA, etc.

**Table 2. VAMHCS HRPP Education and Training Requirements**

Requirement	Verification
Completion of appropriate level of basic education	College transcript, Post-graduate transcript(s) (HR)
Completion of appropriate level of professional training	Transcripts from professional schools (medical, nursing, graduate); VetPro for staff whose education or experience

<sup>26</sup> <http://www.maryland.va.gov/research/training.asp>

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	qualify them for licensure, certification or registration (HR, MSO)
Valid licensure, registration and /or certifications	Current license, registration and/or certification; VetPro
Optional triennial training in Good Clinical Practices	Certificate of completion; CITI
Triennial training in Human Subjects Protection	Certificate of completion; CITI
Annual VA Privacy Policy Web training	TMS
VA Privacy and Information Security Awareness and Rules of Behavior (formerly Cyber Security)	TMS
Mandatory investigator/research staff training sessions	Attendance sheets / certificates
Mandatory investigator/research staff broadcasts	Email responses
Continuing education	Certificates of attendance

## **X Quality Management Plan: Program Oversight**

The oversight of the VAMHCS HRPP generally rests with three major entities: the R&DC, the R&D Service (Office of Human & Animal Research Protections), and the ORC. The Chair of the R&DC answers, through the COS, to the VAMHCS MCD and therefore acts independently of the ACOS/R&D. The HARPO answers directly to the ACOS/R&D and is therefore able to coordinate oversight reports, implement corrective actions and institute program improvements to researchers and research activities conducted at the VAMHCS. The RCO answers directly to the VAMHCS MCD and is therefore independent of the ACOS/R&D and Chair, R&DC.

The role of the R&DC in this respect is summarized in section IV.C.9 of this document and in more detail in HRP 01.03 “Research & Development Committee.” Among its responsibilities, the R&DC annually evaluates the HRPP, including the effectiveness of its subcommittees. The role of the RCO is summarized in section IV.C.7 of this document.

The role of the HARPO is to promote activities to assess and improve the quality, efficiency, effectiveness and compliance of the HRPP, animal and laboratory research programs. The HARPO accomplishes this through evaluation of oversight reports from the ORC, IRB, IACUC, VHA ORO and other sources, followed by implementation of corrective actions plans and program improvements based on observation of needs and opportunities. The HARPO produces written policies and procedures, disseminates information to researchers and research participants, coordinates R&D Service quality

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improvement activities in relation to the VAMHCS, the IRB/IACUC, VHA and other entities.

In addition, the R&D Service routinely evaluates the effectiveness of the IRB through review of IRB minutes at R&DC meetings and audits of IRB functions.

In compliance with VHA Handbook 1200.01, the R&DC annually reviews resources allocated to the Human Research Protections Program and presents recommendations to the MCD and ACOS/R&D. The MCD, in consultation with the COS, ACOS/R&D and RCO adjusts resources to the HRPP as needed.

On at least an annual basis, the R&DC reviews the quality and effectiveness of the IRBs, and the VAMHCS HRPP. Modifications are made as necessary to assure continued relevance of the program to the needs of the service. Revisions to the program are subject to the approval of the VAMHCS ACOS/R&D, the R&DC and the MCD as applicable, and shared with the Executive Performance Improvement Committee. Collaboration with the UMB HRPO and the VAMHCS ORC shall be maintained to ensure harmonization of quality management activities for human research being conducted at the VAMHCS and UMMS.

## **XI Quality Management Program: Guidelines and Resources for Investigators and Staff**

### A. Campus Websites

1. R&D Service Website  
[www.maryland.research.va.gov](http://www.maryland.research.va.gov)
2. UMB Human Research Protections Office website  
<http://hrpo.umaryland.edu/index.html>

### B. Guidelines (Instructional; geared toward investigators and research staff, both experienced or novice)

3. Informed Consent Guidebook (HRP 03.01G)
4. Guidelines for Setting Up a Study Binder and Regulatory Documents Binder (HRP 07.02G)
5. Guidance on Source Documents (HRP 07.03G)
6. Writing Standard Operating Procedures (HRP 07.05G)
7. Study-Specific SOPs (HRP 07.06G)
8. Accepting a Protocol (HRP 07.07G)

- C. Selected Tools & Templates (may be used by investigators as-is or adapted to investigators' needs); are available on the R&D Service website, [http://www.maryland.va.gov/research/human/human\\_subject\\_forms.asp](http://www.maryland.va.gov/research/human/human_subject_forms.asp), or through the R&D Service Office (3D-150),

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10. Worksheets for Submissions to R&DC (Human Studies)
11. Essential and Additional Elements of Informed Consent
12. Lay Language for Informed Consent
13. VAMHCS Informed Consent template
14. VAMHCS HIPAA Tutorial

D. R&D Service Standard Operating Procedures and Process Modules

15. Research & Development Committee (HRP 01.03)
16. Comments, Complaints and Suggestions Related to the Human Research Protection Program (HRP 01.07)
17. Review of Research Documentation for Compliance with Privacy Requirements (HRP 01.12)
18. Information Security Review of Research Protocols (HRP 01.13)
19. Cooperative R&D Agreement (CRADA) (HRP 01.15)
20. Overview of Quality Assurance Activities (HRP 02.01)
21. Investigator Internal Quality Assurance (HRP 02.04)
22. Auditing the Investigational Pharmacy (HRP 02.05)
23. Writing a VAMHCS Informed Consent Form (HRP 03.02)
24. Obtaining and Documenting Informed Consent (HRP 03.03)
25. Research Personnel Training (HRP 04.02)
26. Progress Notes for Research Participants (07.08)
27. PM #036 Advertisements for Non-VA Research
28. PM #040 R&D Service Process Modules and Hot Topics
29. PM #041 Reportable Events-HRPP
30. PM #045 Reportable Events-RISP

E. VAMHCS Policies and SOPs

31. 512-151/R&D-106 Allegations of Research Misconduct
32. 512-119-010 Investigational Drug Section

F. UMB

33. UMB policies and tools are available at the website,  
<http://hrpo.umaryland.edu/index.html>

G. Federal Sources

34. VHA Handbook (1200.01), “Research and Development Committee”
35. VHA Handbook (1200.05), “Requirements for the Protection of Human Subjects in Research”
36. VHA Handbook (1108.04), “Investigational Drugs and Supplies”
37. VHA Handbook (1058.01), “Research Compliance Reporting Requirements”
38. VHA Handbook (1605.1), “Privacy and Release of Information”
39. 45 CFR 46 (DHHS)
40. 38 CFR 16 (VA)
41. 38 CFR 17 (VA)

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H. Other

42. Belmont Report
43. Declaration of Helsinki
44. ICH Guidelines
45. CITI ([www.citiprogram.org](http://www.citiprogram.org).)
46. TMS website ([www.tms.va.gov](http://www.tms.va.gov) )

XII Sources used for this HRPP

A. Federal Sources

1. 45 CFR 46, Subpart A, “The Common Rule” (DHHS)
2. 38 CFR 16 (VA)
3. 38 CFR 17 (VA)
4. 21 CFR 50 (FDA)
5. 21 CFR 56 (FDA)
6. OHRP Guidance, “Engagement of Institutions in Research”, January 26, 1999

B. VA Sources

7. VHA Handbook (1200.01), “Research and Development Committee”
8. VHA Handbook (1200.05), “Requirements for the Protection of Human Subjects in Research”
9. VHA Handbook 1058.01, “Research Compliance Reporting Requirements”
10. VHA Handbook 1605.1, “Privacy and Release of Information”
11. VHA Handbook 1605.2 “Minimum Necessary Standard for Protected Health Information”
12. VHA Handbook 1108.4, “Investigational Drugs”
13. [http://www.va.gov/ORO/ORO\\_Checklists.asp](http://www.va.gov/ORO/ORO_Checklists.asp)
14. VHA Directive 2006-067, “Credentialing of Health Care Professionals” (12/22/06)

C. VAMHCS Sources

16. VAMHCS R&D Service policies and procedures,  
[http://www.maryland.research.va.gov/research/human/human\\_subject\\_sops.asp](http://www.maryland.research.va.gov/research/human/human_subject_sops.asp)

D. External Sources

17. The Belmont Report

XIII. Attachments (follow)

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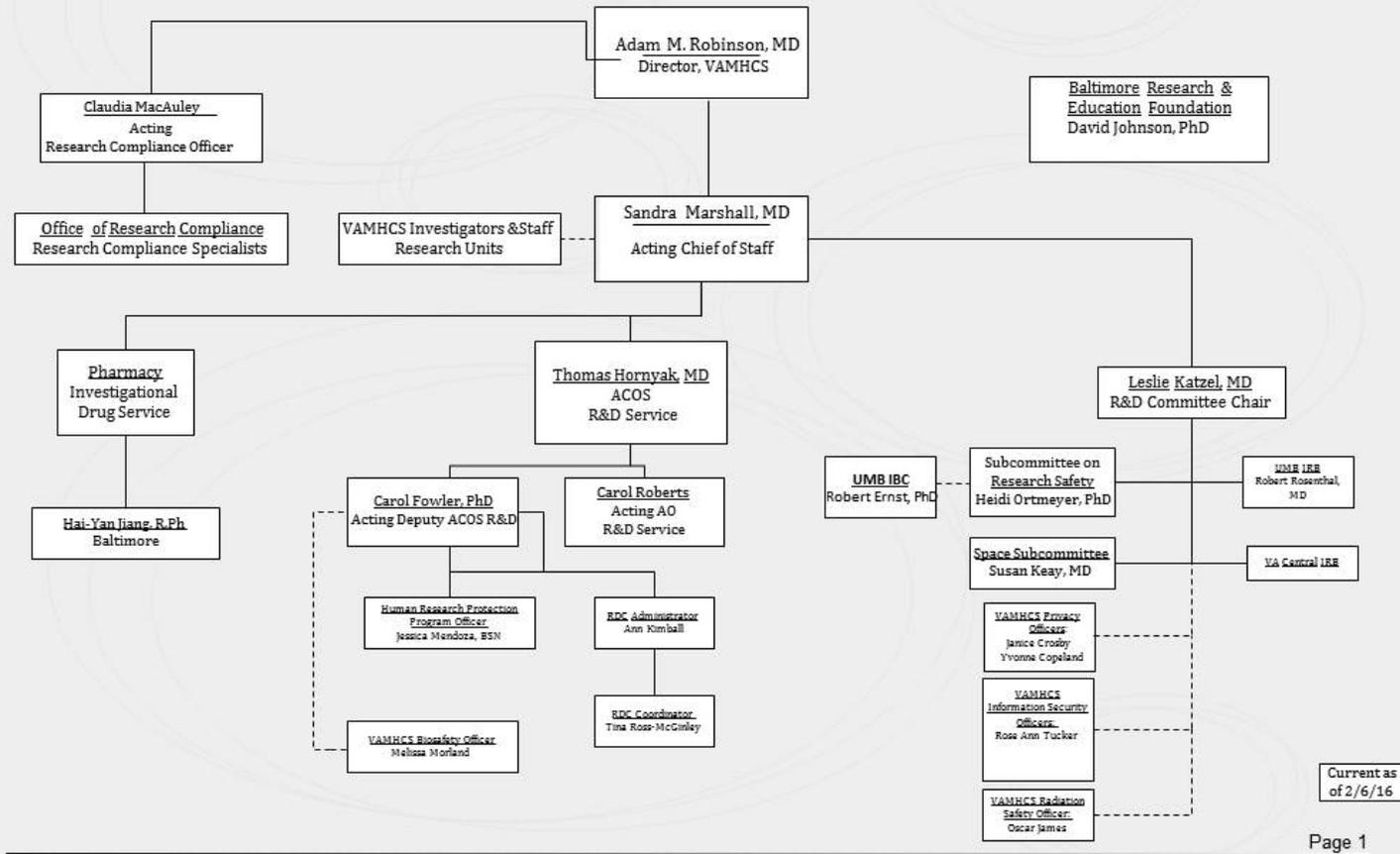
**ATTACHMENT 1:**

**Organizational Structure of Responsibilities for the  
VAMHCS HRPP**

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### RESPONSIBILITIES FOR THE VAMHCS HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

This chart shows the functional/collaborative roles of individuals with regard to the VAMHCS HRPP. It is NOT an organizational chart of supervisory relationships.

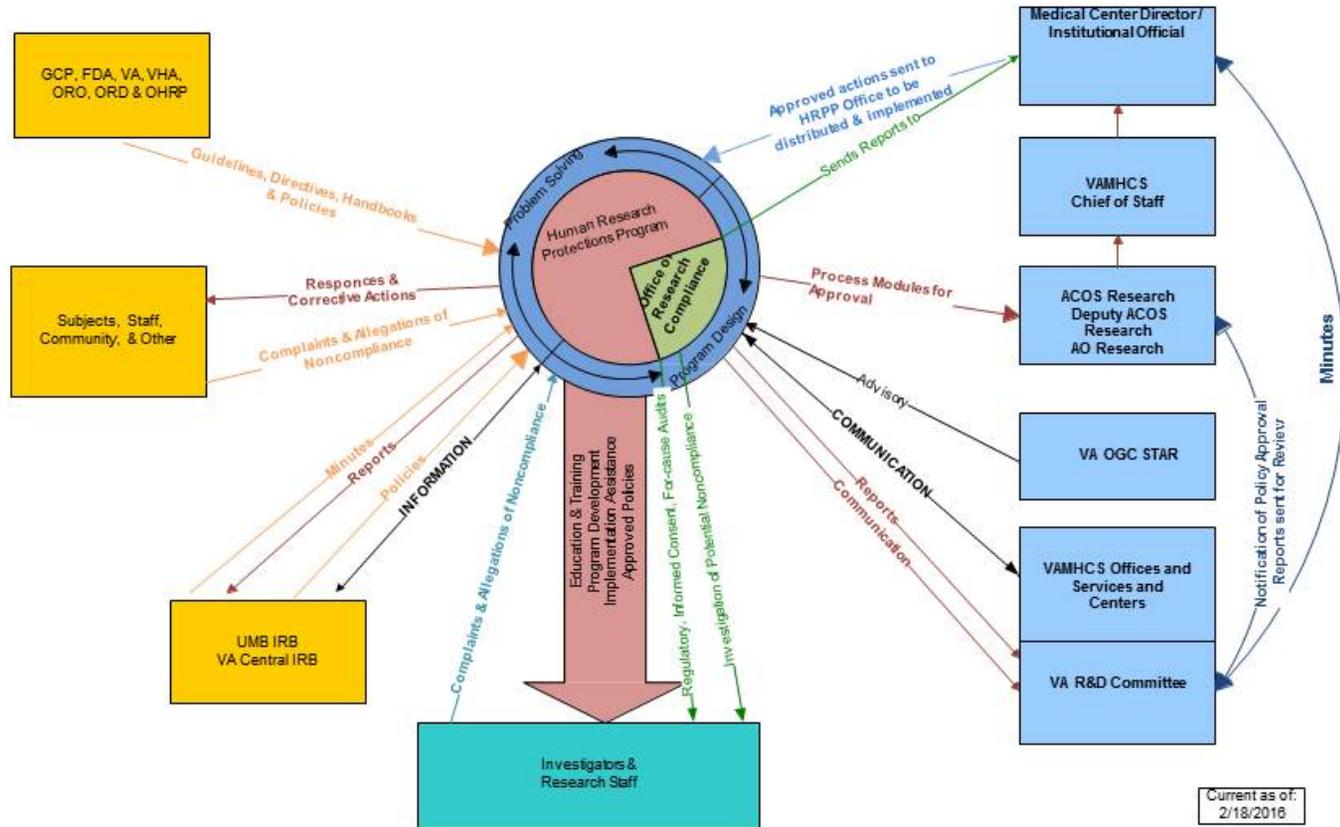


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**ATTACHMENT 2:**

**Flowchart of the Implementation of the VAMHCS  
HRPP**

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**ATTACHMENT 3:**

**VAMHCS Process for Protocol Approval and Study Conduct**

<b>Requirement</b>	<b>Process / Reason</b>
<b>IRB Approval (CICERO)</b>	
CICERO Application	Collects information on the investigators, I/E criteria, requirements for subjects, risk-benefit analysis, justification for the project, description of recruitment and consent processes, study/vulnerable populations, study design & schedule, drugs/devices to be used, advertisements, additional VA requirements, etc. Delineation of VAMHCS v. collaborator activities & elements. Consistency between documents.
Investigator Drug Brochure, Sponsors' protocol, grant	Provides committee with greater detail on scientific merit, potential risks to subjects, pre-clinical findings, etc.
Link to VAMHCS Informed Consent Document template	Must have all essential elements of Informed Consent and applicable additional elements; VA format & requirements.
Link to DSMP Worksheet/Forms	Determines level of safety monitoring that will occur and the process of the monitoring; assist the PI in development of the DSMP.
Link to VAMHCS HIPAA authorization template	HIPAA form is submitted within CICERO; must be submitted unless a waiver is requested.
Amendments (to protocol, ICF, CICERO information)	Submit "Modification Request" to the IRB and R&DC; forms and process through CICERO and via the R&D Service website.
Continuing Review	CR process in CICERO
Study Closure	Submit "Modification Request" to the IRB requesting study closure (only deidentified data being analyzed) or closing of new enrollment.
<b>R&amp;D Approval</b>	
Submission Worksheet	Ensures that all paperwork and sign-offs are provided.
Trainings, Licensing & Credentials	Check of R&D Service tracking systems,

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	HR databases, MSO databases, etc
Amendments (to protocol, ICF, CICERO information) if required for R&DC approval	Submit “Modification Request” to the IRB and R&DC; forms and process through CICERO and via the R&D Service website.
Continuing Review	R&D worksheet and applicable documents
Study Closure	Submit IRB-approved closure; may need to submit “data analysis only” paperwork if analysis of deidentified data will continue.

<b>Recruitment/Enrollment Requirements</b>	
Enrollment Note (Informed Consent Note)	Contains title of study, name of PI, IRB#, IRB dates, date and time ICF was signed, name of the person obtaining informed consent, statement on the participant’s mental status, what information was given, that the subject was able to ask questions, whether legal guardian was involved, etc.
Research Subject Clinical Warning (if applicable)	Contains title of study, contact info of investigators and staff, name of study drug(s)/devices/placebo, expected effect of drug/device, possible adverse effects/toxicities, special instructions, etc.
<b>Study Conduct</b>	
Adherence to protocol	Should be guided by the IRB- and R&DC-approved protocol and the PI’s own internal SOPs and other applicable guidelines; audited periodically by ORC Research Specialists using audit tools; reported to Research Compliance Officer and R&DC and IRB as necessary.
Adherence to DSMP	
Reporting of “Unanticipated Problems Involving Risk to Subjects or Others” and other reportable events	PIs are required to report serious, local ‘Unanticipated Problems’ and other reportable events to the IRB via CICERO when they occur (RNI process) or in continuing review.