

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

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HUMAN RESEARCH PROTECTION PLAN

	ABBREVIATIONS	4
I	Definition of the Human Research Protections Program and Mission Statement	6
	A. Definition of Human Participant	7
	B. Definition of Research	9
	C. Research Conducted, Prohibited or Restricted at the VA	10
II	Policy	11
	A. Ethical Principles Concerning the Protection of Human Research Participants	12
	B. Engagement in Research and Assurances	14
	C. Arrangements for an Institutional Review Board	15
	D. HRPP Document and Related Standard Operating Procedures	16
III	Identification of the Institutional Officer Accountable for the HRPP	16
IV	The Organizational Structure, Process, Roles and Responsibilities for Making Policy to Protect Human Research Subjects	17
	A. Organizational Structure: Responsibilities	17
	B. Organizational Structure: Process	17
	C. Roles	19
	1. Medical Center Director	19
	2. Chief of Staff	23
	3. Associate Chief of Staff for Research & Development (ACOS/R&D)	24
	4. Deputy Associate Chief of Staff for Research & Development (Deputy ACOS/R&D)	24
	5. Administrative Officer for Research and Development (AO/R&D)	25
	6. Research Compliance Officer (RCO)	25
	7. Research Compliance Specialists	27
	8. Research & Development Committee	27
	9. Human Research Protection Oversight & Compliance Subcommittee	29
	10. University of Maryland Institutional Review Board	29
	11. Investigators	29
	12. Research staff	30
	13. Investigational Drug Service and Pharmacy Staff	30

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

	14. Privacy Officer	30
	15. Information Security Officer	31
	16. Executive Performance Improvement Committee	31
	17. Patient Safety/Risk Management Program; Legal Counsel	31
V	Quality Management Program: Overview	32
	A. Policy	32
	B. Purpose	32
	C. Structure	32
VI	Quality Management Program: Privacy & Security	33
	A. Privacy Requirements	33
	B. Data Security Requirements	34
VII	Quality Management Program: Compliance and Quality Assurance of the Human Research Activities of Investigators	34
	A. Approval of a Protocol	34
	B. Conduct of a Protocol	38
	1. Study Closure	39
	C. Oversight of Conduct of a Research Protocol	40
	1. Consent Process	42
	2. Study Conduct	44
	3. Unanticipated Problems Involving Risks to Participants or Others (UPR) and Data Safety Monitoring Plan (DSMP) Conduct and Reports	46
	4. Compliance with Regulations, Policies and Guidelines	48
	5. Investigator Internal policies / Standard Operating Procedures	49
	6. Complaint	49
	D. Actions & Reports	50
VIII	Quality Management Plan: Investigational Drug Service	52
IX	Quality Management Plan: Education and Training	56
X	Quality Management Plan: Program Oversight	59
XI	Long Term Approach	60
XII	Quality Management Program: Guidelines and Resources for Investigators and Staff	61
	A. Websites	61
	B. Guidelines	61
	C. Selected Tools and Templates	61
	D. Selected Forms	62
	E. Research Service SOPs	62
	F. UMB	63
	G. Federal Sources	63
	H. Other	63
XIII	Sources Used for this HRPP	64
XIV	Attachments	66

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

	1. Organizational Structure of Responsibilities for the VAMHCS Human Research Protection Plan	67
	2. Process Flowsheet for the Implementation of the VAMHCS HRPP	69
	3. Federalwide Assurance – VAMHCS	71
	4. Federalwide Assurance – BREF	73
	5. Federalwide Assurance – UMB	74
	6. Memorandum of Understanding – VAMHCS-UMB	75
	7. Table 1: VAMHCS Process for Protocol Approval and Study Conduct	87

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

ABBREVIATIONS

AAHRPP	Association for the Accreditation of Human Research Protections Programs
ACO/R&D	Administrative Officer for Research and Development
ACOS/R&D	Associate Chief of Staff for Research and Development
BRAAN	Biomedical Research and Assurance Network
BREF	Baltimore Research and Education Foundation
CAP	Corrective Action Plan
CFR	Consolidated Federal Register
CICERO	Comprehensive Institutional Evaluation of Research Online
COIO	Conflict of Interest Officer
COS	Chief of Staff
CPRS	Computerized Patient Record System
DQI	Director of Quality Improvement (within the HRPO)
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
HIPAA	Health Insurance Portability and Accountability Act
HRP	Human Research Protection (prefix to applicable Research Service SOPs)
HRPO	Human Research Protection Office (UMB office that administers the IRB)
HRPOC	Human Research Protection Oversight Committee (VAMHCS)
HRPP	Human Research Protection Program
ICF	Informed Consent Form
IDS	Investigational Drug Service
IDP	Investigational Drug Pharmacist
IRB	Institutional Review Board
IRB P&P	Institutional Review Board Policies and Procedures
IT	Information Technology
MCD	Medical center Director
MOU	Memorandum of Understanding
NCQA	National Committee for Quality Assurance
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
QA	Quality Assurance

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

QI	Quality Improvement
QMP	Quality Management Plan
R&D	Research & Development
RCO	Research Compliance Officer
RDC	Research & Development Committee
RMAF	Research Methods Accountability Form
SOP	Standard Operating Procedure
UMB	University of Maryland Baltimore
VAMHCS	VA Maryland Health Care System
UPR	Unanticipated Problem Involving Risks to Participants or Others

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

NOTE: At this time (October 2008) there is a major transition occurring at the University of Maryland Baltimore (UMB) Human Research Protections Office (HRPO):

The UMB IRB's electronic protocol management system will be changing from "BRAAN" to "CICERO". Throughout this document this situation is referred to as "BRAAN/CICERO". This document will be revised as needed once the CICERO system is operational.

I. Definition of the Human Research Protections Program and Mission Statement¹

The VA Maryland Health Care System (VAMHCS)² Human Research Protection Program (HRPP) is a comprehensive and organized system with dedicated resources to ensure the rights, safety and well-being of human volunteers participating in research. The objective of this system 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 is a Memorandum of Understanding (MOU) between the University of Maryland School of Medicine and the VAMHCS that delegates the University of Maryland Baltimore Institutional Review Board as the IRB 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. In general, however, these documents have emphasized prospective protections of research participants (such as with the establishment of Institutional Review Boards for a protocol approval process, the informed consent process, and so on), which are all instrumental in actualizing the ethical principles of beneficence, autonomy and justice.

¹ References and applicable policy memoranda are located in Section XIII: 1-6, 8, 18, 55, 56

² 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 (see Appendix 3, VAMHCS FWA).

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

The VAMHCS HRPP gives equal emphasis to concomitant 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 principals 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 VHA Handbook 1200.5 and other VHA handbooks as they are developed. 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 Research 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 Human Research Protection Program consists of the activities, policies and procedures of the VAMHCS, the University of Maryland, Baltimore (UMB) Human Research Protections Office (HRPO) (including the IRB), the VAMHCS Research Service, and the individuals and committees (i.e. VAMHCS Research and Development (R&D) Committee, and its subcommittees, etc) 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 UMB and VAMHCS research community. 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*** as³:

A human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or

³ VHA Handbook 1200.5, Par 3.g

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

through identifiable private information (38 CFR 16.102(f)). The definition provided in the Common Rule includes investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled. As required by 38 CFR 16.102(f) an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

NOTE [included in the 1200.5 definition]: The FDA definition of human subject differs according to the applicable regulation. See 21 CFR 812.3(p), 21 CFR 50.3(g), 312.3(b,) and 56.102(e).

(*The VAMHCS uses the term "human participant" rather than "human subject" to be compatible with the IRB, DHHS, FDA, and HIPAA terminology.)

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

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

With regard to Health Insurance Portability and Accountability Act (HIPAA)-applicable issues, the definition of “human” extends to the use of decedent’s protected health information.

B. Definition of Research

“Research involving human participants” means any activity that either:

- Meets the DHHS definition of “research” and involves “human participants” as defined by DHHS; or
- Meets the FDA definition of “research” or “clinical investigation” and involves “human participants” as defined by FDA; or
- Meets the VHA definition of “research” and involves “human participants” or human specimens as defined by VHA.

In practice, the VAMHCS has delegated to the UMB IRB the determination of whether the activities constitute “research” involving “human subjects” as defined by the regulations (IRB P&P I.1.A, I.3.C).

DHHS defines **research** as “the 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 this 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 (45 CFR 46.102(d). Examples of systematic investigations include, but are not limited to: observational studies, interviews (including those that are open-ended) or survey studies, group comparison studies, test development, program evaluation; and interventional research.

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.

The IRB defines **research** as:

A systematic investigation, including research development, testing, and

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

evaluation, designed to develop or contribute to generalizable knowledge. **OR** Any experiment that involves a test article and one or more human subjects, and that either is subject to requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 regarding nonclinical laboratory studies. Activities which meet either one of these definitions constitute research for purposes of this 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. Examples of systematic investigations include, but are not limited to:

- a. Observational studies;
- b. Interviews (including those that are open-ended) or survey studies;
- c. Group comparison studies;
- d. Test development;
- e. Program evaluation; and
- f. Interventional research

The VHA definition of research is comparable. In VHA Handbook 1200.5⁴, “Research is defined as the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question. The Common Rule (38 CFR 16) defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. *NOTE (included in the 1200.5 definition): The FDA definition of research differs according to the applicable regulations; see 21 CFR 812.3(h), 21 CFR 50.3(c), 21 CFR 56.102(c), and 21 CFR 312.3(b).*”

C. Research Conducted, Prohibited or Restricted at the VA

The VAMHCS conducts clinical, biomedical, social behavioral, genetic, and database studies. Projects may be investigator-initiated or federally-funded or privately funded and may involve multiple sites, including international sites. Research may involve students (as faculty-supervised investigators or as participants), 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

⁴ VHA Handbook 1200.5, Par 3.v

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

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 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
- Projects involving in vitro fertilization
- 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.

The following categories of research require a CRADO waiver or other special requirements:

- Research involving children
- Research involving prisoners
- International research
- Research involving pregnant women
- Research involving participants with impaired decision making capacity
- Research involving banking of human biological specimens

II. Policy⁵

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. Investigators are bound to conduct their research according to the protocols and procedures approved by their Department Chairs/Service Chiefs, the IRB and the R&D Committee. VAMHCS investigators and staff follow HRPO Policies and Procedures unless additional VAMHCS requirements exist (HRP 01.09).

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

⁵ References and applicable policy memoranda are located in Section XIII: 2, 6, 16-20, 23, 32-33, 53-54.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

2. It is the policy of the VAMHCS that the IRB makes the determination as to whether a research proposal is “human subjects research”, whether the VAMHCS is engaged in research (and VAMHCS staff is 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, whether there is investigator conflict of interest and the COI management plan, the validity of IND and 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 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 RDC 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 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). However, research reviewed and approved by the IRB may be subject to review and disapproval by the MCD or other institutional officials. The MCD and institutional officials may not approve research previously disapproved by the UMB IRB or the R&D Committee (i.e., decisions may not be more lenient than the IRB). The R&D Committee must notify the IRB of all VAMHCS decisions regarding approvals and disapprovals of research.

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.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

Benevolence 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.”

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 benevolence, 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 benevolence. 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 capacity (“Mini-Mental” or other tests), 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 Board (the University of Maryland, Baltimore IRB) and the VAMHCS Research & Development Committee, 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 Research Compliance Office of the Research Service ensures that the VAMHCS research policies are in compliance with applicable sections of the VHA Handbook 1200.1 (R&D Committee), VHA Handbook 1200.5 (Human Research Protections), VHA Handbook 1108.4 (Investigational Drugs), VHA Handbooks 1605.1 and 1605.2 (PHI and privacy), 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 VAMHCS goal of preventing harm to study participants.

VAMHCS HUMAN RESEARCH PROTECTION PLAN (HRP 01.02)

The principles of beneficence, autonomy, and justice are essential tools as the VAMHCS Research 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.

B. Engagement in Research and Assurances

It is the responsibility of the VA Maryland Health Care System (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 Medical Center Director is the Assurance Signatory/Institutional Official and is ultimately responsible for overseeing the protection of human subjects within the facility. The Signatory Official must also ensure that open channels of communication are maintained between the IRB, 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 OHRP Guidance (Jan 1999) as well as in the IRB P&P

I.1.A. 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).

The IRB adds a consideration of “**performance site(s) engaged in research**”:

A performance site becomes “engaged” in human participants’ research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, a performance site is considered to be “engaged” in human

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

participants' research when it receives a direct Federal award to support the research.

A study is VAMHCS research if:

- the research will be conducted completely or partially in VA facilities or at VA approved off-site locations or otherwise utilizes VA resources,
- the research will be conducted by researchers with VA appointments while on official VA duty (including those with WOC status),
- the VAMHCS or its satellites will be recruitment sites for the research project,
- the research is VA-funded, or
- the research involves VAMHCS medical records or VAMHCS databases, or otherwise derives data from intervention or interaction with VAMHCS subjects or tissues.

An “agent” of the VAMHCS is:

Anyone with an appointment to the VAMHCS, whether they are an employee or a “without compensation” (WOC) appointee, and who is engaged in research for the VAMHCS.

C. Arrangements for an Institutional Review Board (IRB)

The VAMHCS has designated the University of Maryland, Baltimore (UMB) IRB as its IRB of record and has established a Memorandum of Understanding (MOU) delineating the responsibilities of the UMB, the VAMHCS and the BREF. The UMB IRB has agreed to comply with 38 CFR 16 and VHA Handbook 1200.5 when reviewing VA research. The VA prohibits the use of commercial IRBs.⁶ The MOU is signed by the University of Maryland School of Medicine Vice Dean for Academic Affairs, the VAMHCS Medical Center Director, the Executive Director of the Baltimore Research & Development Foundation (BREF), and the Network Director, VA Capitol Network, VISN 5 (see Attachment 6 for a copy of the MOU).

The UMB IRB maintains an FWA with DHHS/OHRP (#FWA 00007145, expires June 28, 2010) (Attachment 5). Five IRB panels at UMB are linked to this assurance.⁷ The assurance is signed by the Vice Dean for Research and Academic Affairs, University of Maryland School of Medicine. Each of the five IRB panels reviews all types of research. The UMB IRB currently has one Chair and five Vice-chairs.

The VAMHCS maintains a Federalwide Assurance (FWA): # FWA 00001483, expires October 9, 2010 registered with the DHHS Office for Human Research Protections (OHRP) via the Office of Research Oversight (ORO). This is signed by the Medical Center Director (Attachment 3).

⁶ See IRB P&P I.2.B.

⁷ FWA numbers: 00000233, 00000234, 00000245, 00002923, 00006045

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

The Baltimore Research and Education Foundation (BREF), the VAMHCS non-profit foundation, maintains an FWA with DHHS/OHRP (#FWA 00001420, expires August 24, 2010). This is signed by the AO/R&D in his capacity as Executive Director of BREF (Attachment 4).

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 policies and procedures. The HRPO recognizes that there are VA-specific requirements that VAMHCS staff 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 to VAMHCS Human Research Protection (HRP) Standard Operating Procedures (SOPs), IRB Policies & Procedures, and other documents as needed.

This particular document (HRP 01.02) undergoes annual review but the SOPs and guidelines referenced herein may be on 1 – 3 year review cycles. However, all HRP documents are subject to early review or amendment as necessitated by institutional or regulatory changes.

III. Identification of the Institutional Officer Accountable for the HRPP

The Medical Center Director is the Institutional officer (IO) and is therefore accountable for the implementation and performance of the Human Research Protection Program (HRPP). He is the Institution's signatory on the Federalwide Assurances and Memoranda of Understanding.

The Research Compliance Officer (RCO) has the delegated authority from the Medical Center Director (through the Chief of Staff) for the implementation of the HRPP.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

IV. The Organizational Structure, Process, Roles and Responsibilities for Making Policies to Protect Human Research Subjects⁸

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 Research Service.

While the Medical Center Director (MCD) has ultimate accountability for the HRPP and the Research Compliance Officer (RCO), through the 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: other Research Service administrators, the Office of Research Compliance (ORC), the Research & Development Committee, the Human Research Protection Oversight & Compliance Subcommittee (HRPOC), the Subcommittee on Research Safety, the Radiation Safety Officer, the Privacy Officer, the Information Security Officer, the Investigational Drug Service and the UMB IRB. The Research Compliance Officer and the ORC staff answer directly to the Chief of Staff.

The MCD is ultimately responsible for oversight of the IRB, the Research Service (including the R&D Committee) 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&D Committee.

B. Organizational Structure: Process

While ultimate responsibility for the HRPP rests with the Medical Center Director, most of the development, education, implementation and compliance assessment takes place within the Research Service, particularly in the Office of Research Compliance (ORC). This is illustrated in the flowchart in Attachment 2.

As illustrated in Attachment 2, the ORC is the central point of action for the VAMHCS HRPP. The Research Compliance Officer (RCO) reports directly to the Chief of Staff. However there is collaboration with the ACOS for Research & Development (ACOS/R&D), the Deputy ACOS/R&D and the Administrative Officer for Research & Development (AO/R&D).

The policies that the ORC develops and submits for approval are influenced by policies, regulations, guidance and correspondence from ORO, ORD, OHRP, the FDA, AAHRPP

⁸ References and applicable policy memoranda are located in Section XIII: 7, 8, 11, 14, 18, 19, 21, 23, 32-35.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

and other applicable external agencies. The ORC also uses findings from audits, investigations of complaints and allegations of noncompliance, and other feedback to help develop or revise policies. Research Service policies 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 ORC submits them to the Human Research Protections Oversight and Compliance (HRPOC) Subcommittee of the R&D Committee for review. The HRPOC makes recommendations to the R&D Committee as to the approval of the policy. R&D-approved documents are sent to the Director (MCD) for final approval.

Because the VAMHCS uses the UMB IRB as its IRB of record, VAMHCS researchers and staff must follow UMB policies and procedures unless explicitly stipulated in IRB policies and procedures (IRB P&P). The ORC collaborates with the UMB HRPO to ensure that IRB P&P are compatible with and include all applicable VA regulations and VAMHCS requirements. VA representation by the R&D Committee Chairperson on the UMB IRB executive committee and UMB Advisory Committee for Human Research Policy further facilitates information flow between the two institutions and helps harmonize the SOPs.

Once policies are approved, education of VAMHCS investigators, coordinators and staff begins. This is achieved through the “Research Service Hot Topics” series, 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 individual protocols.

The ORC also serves as a resource for investigators and their staff. It assists them in the development of their own internal policies and procedures, in self-assessments of their own programs and in the institution of Data Safety Monitoring Plans (DSMPs). It also provides guidance and consultation to VAMHCS leadership and research personnel.

The ORC performs routine compliance audits and for-cause audits according to the Research Service SOP, “Overview of Quality Assurance Activities” (HRP 02.01). Results of the compliance program may include audit reports, action plans and follow-up audits and are reported to the R&D Committee, the MCD (through the COS), the ACOS/R&D, the University of Maryland, Baltimore IRB, and, if necessary, OHRP and ORO.

The ORC and VA R&D Committee also perform regular assessments of the UMB HRPO and the Research Service itself. Annual review of the R&D subcommittees by the VAMHCS R&D committee is mandated by VHA Handbook 1200.1. This includes the performance of the IRBs, IRB compliance with VAMHCS policies, relevance and accuracy of VAMHCS and Research Service policies, performance of the R&D Committee and its subcommittees, performance of the Investigational Drug Service, and

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

the competency of Investigators and research staff. 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 Research Service or ORC periodically present educational sessions on VA research matters to the IRB and R&D Committee 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 responsible for the oversight of the HRPP, the IRB and overall research program. As specified by ORO⁹, these responsibilities include:
 - is the Institutional Official responsible for the Facility's compliance with all federal and VA research oversight requirements
 - is responsible for ensuring compliance in research with all requirements for:
 - Security against terrorist events,
 - Inquiries and Investigations of alleged Research Misconduct,
 - Safety and control of infectious agents and radioactive materials,
 - Protection of human research subjects,
 - Care and use of laboratory animals,
 - Control and security of hazardous agents (including select agents and toxins),
 - Granting access to research areas in which hazardous agents are used or stored,
 - Research involving recombinant DNA (rDNA).
 - is responsible for all required reporting to and correspondence with:
 - Federal oversight offices and agencies,
 - Applicable accreditation organizations.
 - is responsible for reporting to the VHA Office of Research Oversight (ORO):
 - Serious or continuing noncompliance in research,
 - For-cause suspensions or terminations of research,
 - Initiation and closure of Research Misconduct Inquiries and Investigations,
 - Adverse events resulting in substantive Institutional Review Board (IRB) action,
 - Adverse events resulting in the unexpected death of a human research subject,
 - Unanticipated problems resulting in substantive IRB action,
 - Any incident that seriously affects the health or safety of laboratory animals.
 - is an *ex officio*, non-voting member of the R&D Committee and attends R&D Committee meetings as appropriate.

⁹ <http://www1.va.gov/oro/docs/Facility-Director-Cert-Checklist-032307.doc>

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

- appoints, or ensures the appointment of the required research oversight personnel and committees in writing and in accordance with VHA requirements:
 - Associate Chief of Staff for Research (ACOS/R)
 - Permanent Research Integrity Officer (RIO) for Research Misconduct.
 - R&D Committee Chair (1-year renewable term) and members (staggered 3-year renewable terms) who reflect the Facility’s research program
 - VA representatives of the IRB (through nominations to the IRB).
 - VA representatives of the Institutional Animal Care and Use Committee (IACUC) (through nominations to the IACUC).
 - Subcommittee on Research Safety (SRS) Chair (1-year renewable) and members (specified terms required).
 - Alternative Responsible Official (ARO) or AROs with specified duties related to control of hazardous agents in research laboratories.
 - Representatives to academic affiliate committees.
- Ensures the appointment of:
 - Research Misconduct Inquiry/Investigation Committee members.
 - Radiation Safety Officer.
 - Research Safety Coordinator
 - Biological Safety Officer (BSL-3 rDNA research; rDNA research with viable organisms).
- Certifies 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:
 - Human Research Protection Program (HRPP),
 - Animal Care and Use Program (ACUP),
 - Research Safety and Security Program (RSSP),
 - Research Safety Program
 - 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)
 - Research Service Education Plan
 - Animal Facility Disaster Plan
 - SOPs for Financial Conflicts of Interest in Research
 - SOPs for R&D Committee
 - SOPs for the IRB
 - SOPs for the IACUC
 - SOPs for the SRS
 - SOPs for other R&D Subcommittees

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- SOPs for Destruction of Select Agents and Toxins, including Exempt Quantities
- BSL-3 Laboratory Safety Manual
- SOPs for Research Misconduct
- Certifies that the Facility’s research oversight programs have sufficient resources and administrative support to maintain active fulfillment of their responsibilities, including sufficient personnel, space, equipment, engineering support, and technical assistance
 - HRPP, ACUP, RSSP, Hazardous Agents Control Program, Occupational Safety and Health Program, and Research Integrity Program
 - R&D Committee, IRB, IACUC, SRS, other R&D Subcommittees, Research Misconduct Inquiry/Investigation Committees, and other research oversight entities
- Certifies 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;
 - RIO (and Research Misconduct Inquiry/Investigation Committee members as needed);
 - All relevant individuals to ensure knowledge of responsibilities for reporting:
 - Loss or compromise of keys, passwords, combinations, etc.
 - Suspicious persons or activities
 - Loss, release, or theft of select agents or toxins
 - Alteration or compromise of inventories or records for select agents or toxins;
 - Facility Director for Federalwide (Human Subject) Assurance (FWA)
 - ACOS/R and Administrative Officer for Research (AO/R)
 - R&D Committee and applicable Subcommittee members (e.g., IRB, IACUC, SRS)
 - All persons administering, working in, or (as warranted) visiting research laboratories to:
 - Ensure safety and security of select agents, toxins, and other hazardous agents
 - Convey the laboratory’s Emergency Preparedness and Response Plan;
- Certifies that all of the Facility’s required research assurances, authorizations, accreditations, and memoranda of understanding (MOUs) are current, accurate, and complete:
 - FWA and IRB registration(s)
 - Public Health Service (PHS) Animal Welfare Assurance
 - Accreditation by Association for the Accreditation of Human Research Protection Programs (AAHRPP)
 - Accreditation by the Associate for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)
 - Certificate(s) of Registration from APHIS or CDC for use or storage of select agents or toxins
 - Verification that other entities with which the Facility conducts human research hold appropriate human protection Assurances;
 - Approval of the Chief Research and Development Officer (CRADO) for research involving children, prisoners, access to VA records by non-VA employees, and

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- international research involving human subjects, human biological specimens, or human data,
- Authorization from the Under Secretary for Health (USH) for research invoking the Common Rule exemption for research involving public benefit or service programs;
 - Approval of the Chief Veterinary Medical Officer in the VHA Office of R&D for any animal facility construction or renovation costing over \$100,000;
 - MOU(s) for the use of the UMB IRB and IACUC;
 - Cooperative R&D Agreements (CRADAs) other written agreement(s) for collaborative research projects or research oversight arrangements.
- Certifies 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, Privacy Officer, and/or Information Security Officer (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
 - Annual Certification of Research Information Security Requirements
 - Submission in a timely fashion of all required reports to oversight and accreditation bodies
 - Review by the Director of:
 - Annual R&D Committee Program Review, including:
 - Review and recommendations regarding budgetary and resource needs
 - As applicable: Review of the HRPP, ACUP, RSSP
 - Review of all R&D Subcommittees (internal and external)
 - Review of compliance with relevant credentialing, training, and personnel requirements, including Without Compensation (WOC) requirements
 - Quality Assurance (QA) review of publications listing VA support and affiliation
 - QA review of CRADAs
 - Semi-Annual Inventory of Hazardous Agents
 - Semi-Annual IACUC Program and Facility Self-Assessment
 - IACUC reports on allegations of improper animal care and use;
 - Receipt and review by Director of:
 - Meeting Minutes for R&D Committee and all R&D Subcommittees
 - Research Misconduct Inquiry and Investigation Committee recommendations and reports
 - Annual Vulnerable Assessments of all research laboratories
 - Annual safety inspections and annual emergency preparedness and response drill to evaluate the Facility Safety Plan
 - Annual compliance inspection of each laboratory with select agents or toxins

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- Annual SRS review and R&D Committee Approval of Service-wide Safety Manual
- Annual Occupational Safety and Health inspection of research space
- USDA Annual Report of Research Facility
- Annual VA Veterinary Medical Unit Report
- Semi-Annual Review of status of persons authorized to enter areas where select agents or toxins are used or stored
- Reports of monitoring programs to ensure the safety of research subjects;
- Submission of Research Misconduct Inquiry and Investigation Reports and Director's recommendations to VISN Director
- Implementation of Action Plans to correct identified noncompliance with VHA or other federal research oversight requirements
- To accomplish these tasks, the MCD:
 - Delegates authority to administer the R&D program to an appropriately experienced individual, through the Chief of Staff (COS) ([VHA Handbook 1200.5](#)) to the Associate Chief of Staff for R&D (ACOS/R&D);
 - Implements R&D program, policies, and procedures;
 - Establishes and appoints members of the R&D Committee and subcommittees;
 - Ensures that the affiliate agrees to abide by VA policy, including the education and knowledge base to review research in accordance with ethical standards, and that at least two members of each review committee of the IRB are from the VA;
 - Ensures that R&D funds are not used for routine clinical care or administrative support services that should be provided by the medical center (i.e., radiation safety, infection control, library supply, personnel management, fiscal, facility engineering, or building management);
 - Uses the R&D portion of VERA funds to provide indirect support for research;
 - Provides adequate administrative support for the R&D Committee, Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), and the Biosafety Subcommittee, including personnel, space, and time to conduct research activities during their VA tour of duty;
 - Provides adequate administrative support for the HRPP including space, personnel, training & education, materials, and capital equipment;
 - Ensures that the research program reimburses the medical care appropriation for clinical services provided as a result of research: ([38 CFR §17.101\(g\)](#));
 - Ensures the ethical conduct of research and that adequate safeguards are in place to protect human subjects, including the education and knowledge bas of investigators and staff to conduct research in accordance with ethical standards and applicable regulations.
- To avoid possible conflict of interest among institutional officials, the Medical Center Director may not serve as a voting member of the IRB or the R&D Committee.

2. The Chief of Staff:

- Oversees R&D functions;
- Supervises the RCO;

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- Meets regularly with the Research Compliance Officer on activities of the Office of Research Compliance;
 - Receives reports from the Research Compliance Officer, the Executive Performance Improvement Committee, the ACOS/R&D, and the R&D Committee;
 - Reports to the Medical Center Director;
 - To avoid possible conflict of interest among institutional officials, the Chief of Staff may not serve as a voting member of the IRB or the R&D Committee.
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 research and for human and animal subjects' research protection;
 - Administration of the facility's R&D program, including the operations of the R&D Committee and subcommittees;
 - Participation with the Medical Center Director 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;
 - Maintenance of liaison with the Dean's Committee or Medical Advisory Committee;
 - Assisting investigators by providing advice and guidance in administration and technical matters;
 - Aiding in the recruitment, appointment, and employment of R&D personnel; the progress review of investigators' R&D programs; and review of publications, scientific exhibits, and public information releases of R&D activities;
 - Dissemination of educational materials to all investigators with active or planned research programs, IRB members, IACUC members, and R&D Committee members;
 - Preparation, submission, and maintenance of communications, reports, and correspondence required for the administration of the facility's R&D program;
 - Financial management of the facility's R&D program;
 - Supervision of contracts when requested;
 - To avoid possible conflict of interest among institutional officials, the ACOS/R&D may not serve as a voting member of the IRB or the R&D Committee.
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, VA Central Office, and other external bodies as needed;

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- Systematically reviews and reports on such administrative functions as manpower utilization, personnel, training, space utilization, publications, supply procedures, and reports;
 - Develops and implements control procedures for fiscal matters, supplies, equipment, and services such as common resources, and animal facilities;
 - Sits on the Human Research Protections Oversight Committee (HRPOC);
 - 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;
 - 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 Research Service programs;
 - Presents the Institution's Chief Financial Officer with requests for funding;
 - Reports the budget analysis to the R&D committee at least annually;
 - Assisting such administrative functions as recruitment of staff, personnel actions, preparation of reports by investigators, provisions of facilities for the R&D Committee and its subcommittees, and preparation of reports by the ACOS/R&D;
 - Supervising nonprofessional staff members when requested by the ACOS/R&D;
 - Performing other related functions as assigned by the ACOS/R&D.
6. The Research Compliance Officer (RCO) reports to the Chief of Staff. Under limited supervision, uses subject matter expertise to develop, implement and evaluate VAMHCS-wide regulatory compliance and quality management programs pertaining to human subjects research. The RCO is responsible for:
- Primarily, developing and implementing a comprehensive research compliance monitoring plan to assess effectiveness of human subject protections at the VAMHCS in conjunction with UMB;
 - Performing follow-up assessments and actions regarding the implementation of the VAMHCS Human Research Protection Plan (HRPP);
 - Administering the Office of Research Compliance (ORC) including its staff of Research Compliance Specialists and others who comprise the Quality Management Team;
 - Evaluating the institution's adherence to applicable federal regulations, state laws and accreditation standards, which govern human research;
 - Monitoring changes in VA and other federal regulations, policies, manuals and handbooks through tools such as the OHRP listserv, ORD directives, ORO communications, and HRPO communications;
 - Evaluating the R&D Committee's adherence to applicable federal regulations, state laws and accreditation standards, which govern human research;

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

- Evaluating the IRB’s adherence to applicable federal regulations, state laws and accreditation standards, which govern human research;
- Evaluating investigators’ and research staffs’ adherence to applicable federal regulations, state laws and accreditation standards, which govern human research;
- Recommending to the Research and Development Committee (RDC) and senior Medical Center leadership(MCD, COS), suspension of research studies if significant non-compliance or scientific misconduct is uncovered;
- Suggesting systematic 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;
- Formulating institutional policies regarding protection of human research subjects;
- Working closely with other departments and entities including Biosafety (including the Animal Care Facility and the BSL-3 laboratory), 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;
- Evaluating the outcome of the institution’s systematic changes that impact the conduct of human research and provide information to the R&D Committee and the Medical Center Director as to whether these changes have lead to improvements;
- Participating in the training, education and development of individuals responsible for the oversight or conduct of human research;
- Assisting investigators in the development and implementation of their DSMPs and other aspects of their Quality Management Plans;
- Overseeing the conduct of the internal auditing program for VAMHCS protocols;
- Responding to subject or staff complaints;
- Spearheading, in collaboration with the HRPO and the IACUC, the investigation of allegations of human subjects research noncompliance, including, as necessary, the sequestration and analysis of research records and materials, and preparation of materials necessary to conducting, documenting and reporting the investigations;
- Collaborating and communicating with the IRB Executive Committee regarding issues pertaining to the VA, matters of research noncompliance, quality deficiencies, and corrective actions;
- Responding to reports or findings of non-compliance by investigators;
- Reporting findings, activities and proposals to the MCD, ACOS/R&D, the R&D Committee, the Executive Committee, and the University of Maryland, Baltimore IRB;
- Acting as the VAMHCS Research Conflict of Interest Officer;

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- In conjunction with the IRB and as needed, reporting unanticipated problems, adverse events and deficiencies to the FDA, OHRP/HHS, ORO, VA Central Office, other VAMC officials, the Sponsor, and other patients;
 - Reporting “imminent adverse experiences”^{*} to ORO as needed;
 - Acting as the liaison between the VAMHCS Research Service (including the R&D Committee and the Human Subjects Subcommittee) and the UMB IRB;
 - Reporting the minutes of IRB meetings to the R&D Committee;
 - Evaluating the performance and documentation of IRB meetings and operations;
 - Acting as a resource for investigators and staff;
 - Reviewing reports of Unanticipated Problems Involving Risks to Participants or Others (Adverse Events) and DSMPs from PIs via BRAAN/CICERO;
 - Assisting the UMB IRB with AAHRPP certification;
 - Sits on several Data Safety Monitoring Boards;
 - Is an ad hoc (non-voting) member of the UMB IRB and is a non-voting member of the R&D Committee.
7. The Research Compliance Specialists in the Research Compliance Office are responsible for:
- Assisting in the development and implementation of a comprehensive research compliance monitoring plan to assess effectiveness of human subject protections at the VAMHCS;
 - Assisting, on an as needed basis, investigators/divisions/departments to develop unit and protocol specific research quality management plans and/or DSMPs;
 - Working with the Research Compliance Officer to develop priorities and strategies for disseminating information on all areas of human subjects research regulatory compliance to the campus research community;
 - Acting in the capacity of Research Compliance Officer when the RCO is absent;
 - Performing for-cause and annual audits of investigator compliance with GCPs and institutional policies & procedures;
 - Developing institutional corrective action plans (CAPs);
 - Developing standard operating procedures;
 - Participating in activities essential to ascertain and maintain AAHRPP Accreditation of VAMHCS’s Human Protections Program.
8. The Research & Development Committee (RDC)¹⁰ is responsible through the Chief of Staff, to the Medical Center Director for maintaining high standards throughout the facility’s R&D Program. The R&D Committee 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, laboratory safety, and welfare of animal subjects in R&D. It advises the Director on professional and administrative aspects of the R&D Program. All R&D activities

^{*} See page 47 for definition.

¹⁰ See “R&D Committee” (HRP 01.03)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

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;
- Evaluating critically the quality, design, desirability, and feasibility of each new R&D proposal, amendment to an approved protocol, continuing R&D project, application for funding, manuscript to be submitted for publication, or other reporting activity to assure maintenance of high scientific standards, protection of human subjects, adequate safety measures, and proper use of animal subjects;
- Evaluating research proposals for their relevance to veterans' health and to the missions of the VA and the VAMHCS;
- Evaluating critically the effectiveness of the Human Research Protections Program (HRPP) including its compliance with human subjects protections standards, its outreach to researchers and participants, and its needs.
- 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;
- Advising the Director on the recommendation to the Chief Research and Development Officer of candidates for the position of Associate Chief of Staff for Research and Development;
- Evaluating the reports and approving the actions of the Human Research Protection Oversight & Compliance Subcommittee, and other 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;
- Setting institutional policy for training of research personnel;
- 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 Medical Center Director;
- 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 Privacy Officer (PO) and Information Security officer (ISO).as non-voting members pf the RDC;
- Following the principles, objectives, and functions outlined in VHA handbook 1200.1, the R&D committee will establish subcommittees on Human Studies [Institutional Review Board (IRB)], Animal Studies [IACUC], Grant Review,

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- Space and Research Equipment, and Research Safety. These subcommittees will advise the R&D Committee on matters relating to each subcommittee. No research may be undertaken without R&D Committee and appropriate subcommittee(s) review and approval.
- Following the parameters set forth in the Research Service SOP, “R&D Committee” (HRP 01.03), including conflict of interest of committee chairs and members;
 - The ethical conduct of research and for human and animal subjects research protection.
9. The Human Research Protection Oversight and Compliance Subcommittee (HRPOC) is a subcommittee of the R&D Committee. It is responsible for the comprehensive review of VAMHCS policies and procedures already in existence and for the development of new policies and guidelines for the protection of human subjects. Its roles are:
- To make assessments of the Institution’s current program’s strengths and weaknesses;
 - To initiate actions to improve the protection of human subjects in VAMHCS research programs; this includes the development of needed policies and procedures for all staff involved in human subjects research as well as providing ongoing education and consultation to improve ongoing research programs;
 - To act in a consultative role regarding program accreditation activities;
 - To report to the R&D Committee with minutes and reports going to the Medical Center Director.
10. The University of Maryland Institutional Review Board, an entity of the UMB Human Research Protections Office, is the VAMHCS IRB of record. 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. Investigators are ultimately responsible for their research protocols and the protection of the subjects enrolled in them.¹¹ 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;
 - To follow proper informed consent procedures;
 - To ensure that they and their staff are knowledgeable about and follow all applicable VAMHCS and IRB SOPs, policies and procedures;

¹¹ See “Conducting Human Participants Research at the VAMHCS: The Relationship of VAMHCS Research Standard Operating Procedures to the Policies and Procedures of the UMB Human Research Protections Office (HRPO)” (HRP 01.09)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- 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.

12. 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;
- 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.

13. Investigational Drug Service (IDS) and other Pharmacy Staff are responsible for adhering to policies and procedures for the receipt, storage, preparation, documentation and dispensing of investigational drugs (VHA Handbook 1108.4; VAMHCS SOP 119-010; Research Service SOP HRP 05.01).

14. Privacy Officer (PO)¹² 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&D Committee as a non-voting member;
- Reviewing all human research protocols for privacy criteria as a requirement for R&D Committee approval ;
- Raising privacy issues directly to the R&D Committee.

¹² See “Review of Research Documentation for Compliance with Privacy Requirements” (HRP 01.12)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

15. Information Safety Officer (ISO)¹³ 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 individually identifiable information (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&D Committee as a non-voting member;
 - Reviewing all human research protocols for information security criteria as a requirement for R&D Committee approval (including Appendixes C and D);
 - Raising IT issues directly to the R&D Committee;
 - 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.
16. The Executive Performance Improvement Committee (EPIC), an arm of the Office of the Chief of Staff, reviews quarterly and annual reports on research compliance activities, presented by the Research Compliance Officer. This is an additional mechanism whereby senior Medical Center management maintains oversight of the HRPP.
17. The Patient Safety/Risk Management Program and Institutional Legal Counsel provide the Research Compliance Office with information, notification of problems (such as complaints, violations of policy, allegations of noncompliance), and guidance toward proper remediation.

¹³ See “Information Security Review of Research Protocols” (HRP 01.13)

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)****V. Quality Management Program: Overview****A. Policy**

The VAMHCS Research & Development (R&D) Service maintains an integrated quality management program (QMP) outlined in a written plan (see sections VI-XIII). This plan is subject to annual review. Interim modifications to the plan may be made as warranted by regulatory changes and program needs.

The provisions of the QMP apply to all research involving human subjects that is conducted in VAMHCS facilities, conducted in approved off-site locations/facilities, uses VA data and/or conducted by VAMHCS researchers while on official duty. The research may be VA funded, funded from extra-VA sources, or conducted without direct funding.

B. Purpose

- To monitor and assess the implementation of the Human Research Protection Plan (HRPP) and to institute programmatic changes as necessary
- To establish a defined guidance in the conduct and operation of a comprehensive and integrated quality management program (QMP)
- To support the mission and philosophy of the R&D Service (see section I)
- To support the function of the R&D Committee and its subcommittees
- To comply with the requirements of external accrediting agencies as applicable
- 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:

- Tracking systems and databases with the capacity to identify the site and investigator for each research project and allied members of the research team (BRAAN/CICERO, PROMISE);
- Tracking systems/databases with the capacity to track investigators', research staff's and subcommittee members' mandatory human subjects protections trainings;
- Staff performance measures in the form of documented scopes of practice. As applicable, some clinical staff will be subject to the credentialing and privileging processes within VAMHCS. Collaboration with Human Resources is advised;
- A review process to evaluate investigator compliance to the research protocol and, as applicable, privileges/scope of practice and/or defined limitations for

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

each investigator and/or allied research staff related to protocol implementation;

- A review process to evaluate investigator compliance with informed consent procedures and documentation;
- 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;
- An auditing process directed to assessing the quality of regulatory compliance and protocol implementation by the investigators and other allied research staff;
- A review process to evaluate the effectiveness of research policies and procedures.

VI Quality Management Program: Privacy and Data Security¹⁴

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. Both the UMB (through the IRB) and the VAMHCS (through the R&D Committee review process) evaluate the privacy risks of research proposals and must approve HIPAA documents and privacy protection plans according to established policies and procedures.

In compliance with VA mandates, the VAMHCS has named a Privacy Officer (PO) who (among other Medical Center duties) sits on the R&D Committee for the purpose of reviewing research proposals to ensure that the privacy requirements have been satisfied. The PO reviews each research proposal 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 waivers, and other required elements. All human research protocols must receive PO approval in order to be approved by the R&D Committee. The R&D Committee 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.

¹⁴ References and applicable policy memoranda are located in Section XIII: 9-10, 30-31.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

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 an Information Security Officer (ISO) who (among other Medical Center duties) sits on the R&D Committee for the purpose of reviewing research proposals to ensure that information security requirements have been satisfied. The ISO reviews each research proposal 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 receive ISO approval in order to be approved by the R&D Committee. The R&D Committee 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)¹⁵

A. Approval of a Protocol

The VAMHCS Quality Management Program begins with the protocol submission process. A summary of specific steps in the approval process is illustrated in Attachment 7. In order for a human subjects protocol to be approved, a VAMHCS investigator must pass materials through both the University of Maryland IRB, the VAMHCS R&D Committee and its applicable subcommittees, all of which incorporate mechanisms for approving only those protocols which have scientific merit and which can be conducted without undue burden or risk for subjects. VAMHCS R&D Committee members and IRB members are required to have training in human research protections, GCPs and HIPAA.

No VAMHCS research can begin until both IRB and R&D Committee approvals have been obtained. The IRB is responsible for decisions on 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.

¹⁵ References and applicable policy memoranda are located in Section XIII: 13, 20, 22-23, 29, 34-3740, 45-51, 53-54.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

Tools and checklists to assist research staff with writing and submitting protocols and informed consent documents are available through the Research Service and IRB websites.

Both the IRB and the R&D Committee require that Department Chairs or their designees 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. Conflict of interest (COI) is also addressed and the IRB approves COI management plans as described in IRB P&P I.1.G.

The IRB considers the scientific merit of the project,¹⁶ the quality of the informed consent document, and the balance between risks and benefits for subjects. The BRAAN (Biomedical Research and Assurance Network) system, a paperless protocol submission process which went on-line on the UMB/VAMHCS research campus on 9/15/03, prompts investigators to populate information into the “BRAAN Protocol” and into the Informed Consent Document template. The BRAAN submission must be signed by the investigator’s department head(s) (who should review it for scientific merit and feasibility) before it can be passed through (via BRAAN) to the IRB’s “Deferral Prevention Program”. In the summer of 2008, the BRAAN system is to be replaced by an improved and updated protocol management program: “Comprehensive Institutional Evaluation of Research Online” (CICERO).

Once at the IRB, the Deferral Prevention Program (begun in 2005) is triggered. Teams of Quality Improvement Specialists and IRB Analysts review all incoming business for immediate triage (to expedited or full board review) and administrative “pre-review”. The goal of the administrative “pre-review” is to correct clerical errors, request missing information, ensure regulatory requirements and address other issues that would result in the protocol being tabled or deferred. In this way IRB committee members are more likely to have accurate presentations of research proposals for their deliberations and protocols are more likely to move efficiently toward final decisions on approval or rejection. The deferral prevention program also encourages the IRB reviewers to direct questions to the investigators (via the IRB analysts) prior to the convened IRB meeting on issues that require clarification. This provides the PIs the opportunity to address “unknowns” prior to the meeting, and further reduces the number of protocols that require deferral.

The R&D Committee, through its reviews and the recommendations from its subcommittees, considers the scientific merit of the proposal, the logistics and funding for the project, the quality of the informed consent document, and the balance between risks and benefits for subjects¹⁷. It requires information on the expertise of the

¹⁶ IRB P&P I.1.B “Department or Entity Scientific and Feasibility Review of Initial Submissions for IRB Review and Determination”

¹⁷ HRP 01.03 “Research & Development Committee”

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

investigator and staff who will be administering medications, performing procedures, or using equipment. Protocols are also reviewed by the Investigational Drug Pharmacist, the Information Security Officer, the Privacy Officer, the Research Compliance Officer, and the Radiation Safety Officer as well as other applicable entities such as Hospital Epidemiology, Pharmacy & Therapeutics, and Risk Management. The R&D Committee 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 study personnel 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.

Chairs and members of the R&D Committee and subcommittees who have a conflict of interest are prohibited from participating in the initial review, review of amendments, continuing review, and review of adverse events and UPR of those research protocols. Committee/subcommittee members and Chairs complete financial disclosure forms which are kept on file in the Research Service Office under the control of the Research Service COI Officer. The Chair or member(s) with a conflict of interest will verbally disclose the conflict of interest to the R&D Committee Chair or Co-chair or subcommittee 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&D Committee or subcommittee. The 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&D Committee or subcommittee meeting.

In general, all investigator COIs should have been identified and managed prior to R&D committee review (see IRB P&P I.3.G). If, during the process of VA R&D submission, a new or unresolved conflict of interest is identified, the VA R&D Committee will not grant final approval to any VA research activity until documentation has been received from the VAMHCS Conflict of Interest Officer that the conflict has been managed and/or resolved. The VAMHCS Research COI Officer (COIO) notifies the IRB of the potential COI; the IRB proceeds according to its P&P I.3.G.; and the Research COIO reports the IRB's management plan to the R&D Committee. Investigators must disclose and manage COI in the manner approved by the IRB. Nationwide, the VA Central Office is in the process of developing VA specific COI policies. Once these VA policies are established, the VAMHCS will form its own COI committee. This COI committee will also address potential institutional (VAMHCS) COI. In the interim, the RCO has been designated as the Research Conflict of Interest Officer for the VAMHCS.

The Investigational Drug Pharmacist (IDP) is a permanent member of the VAMHCS R&D Committee, 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 are through the Investigational Drug Service except for a few specialized cases where this is not feasible. If it is necessary for the investigator to dispense study drug(s), there must be

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

a written plan that is approved by the IDP and the Chief, Pharmacy Services (VAMHCS SOP NO. 119-010).

If the study entails the use of investigational drugs/placebos, devices, or procedures, a “Research Methods Accountability Form” must be submitted to the R&D Committee. The Research Methods Accountability Form is a mechanism by which the IDP (1) is notified of research projects in which study drugs will be administered to study subjects (2) can prepare for and approve special storage or handling procedures.

Similarly, the Attestation for the Use of Devices notifies safety committees/agents about the potential use of investigational devices on or in VAMHCS patients or on VAMHCS premises. Attestations for procedures and equipment¹⁸ must also be submitted if *any* study-related procedure or equipment (*even if the procedure or equipment is not investigational*) will be used specifically for the study. In this way investigators take responsibility for the proper training of staff that will be performing study-related procedures and for proper storage, maintenance, and operation of equipment.

During the course of a study, it is often necessary to amend the protocol, the informed consent form, the logistical details provided in the BRAAN/CICERO submission, or other aspects of the study. In this case, investigators must submit a “Modification Request” to both the IRB and the R&D Committee. The IRB and the R&D Committee review and approve modifications in similar fashion to that described for initial submission.

As part of the IRB submission, the BRAAN/CICERO system triggers the PI to submit a Data Safety Monitoring Plan (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.

As the study proceeds, the Office of Research Compliance may include audits of DSMPs in its routine monitoring activities. The Research Compliance Officer and Research Compliance Specialists have “read-only” access to BRAAN/CICERO for VAMHCS protocols in order to examine investigators’ annual, DSMP, and UPR reports. The Research Compliance Officer may also receive DSMP reports from PIs via their annual reports to the IRB. The Research Compliance Officer can thus be involved in remediation as needed. The Research Compliance Officer reports DSMP activities to the R&D Committee and the IRB. The Investigator must also report (and the Research Compliance Officer also reviews) occurrences of UPRs according to IRB P&P. Further details on DSMPs on campus and on UPR reporting are found in the relevant IRB P&P (I.3.J).

¹⁸ “Attestation for the Use of Equipment in the Conduct of a Research Study”, “Attestation for the Performance of Procedures in the Conduct of a Research Study”, “Attestation for the Use of Devices”

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

B. Conduct of a Protocol

Recruitment of potential subjects may not begin at the VAMHCS until the protocol has been approved by the UMB IRB and VAMHCS R&D committee. In the BRAAN/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&D Committee-approved VA (10-1086) research informed consent forms. In general, a potential subject may not be screened for participation in a study until a process of informed consent has concluded with a signed informed consent form¹⁹. The PI may formally delegate qualified staff to perform the informed consent process²⁰. The PI must provide a detailed description of the informed consent process in the BRAAN/CICERO protocol. Under certain circumstances, the IRB may grant a waiver of written informed consent (see IRB P&P II.7.E and VAMHCS HRP 03.01G).

When subject recruitment begins, investigators/staff are required to enter consent notes, enrollment notes, and research notes into participants' electronic medical records (CPRS). Soon after this, copies of the signed informed consent forms and HIPAA Authorizations must be brought to the Research Service whose staff then scans the copies into CPRS, ensuring that clinical staff has access to information regarding the study. In addition, a "Research Subject Clinical Warning" must be placed in the subject's electronic medical chart (CPRS) unless one of the following applies²¹:

- The subject's participation in the study involves only the use of a questionnaire or the use of a previously collected biological specimens;
- The identification of the patient as a subject in a particular study would place the subject at greater than minimal risk;
- If a Certificate of Confidentiality has been obtained for the protocol.

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, should be registered in CPRS unless they fit the criteria above. This allows consent forms to be scanned into the medical record, research progress notes to be recorded, and laboratory tests to be performed and reported. It also allows the participant to be pre-registered in the VA system in case treatment for unanticipated events related to the research is necessary.

¹⁹ Studies that are granted, *by the IRB*, a HIPAA waiver or a partial privacy waiver, may screen patients prior to obtaining informed consent (IRB P&P II.6.B).

²⁰ Staff must have completed required GCP and VHA privacy training; must be within staff's scope of practice; must be formally designated by the PI in BRAAN/CICERO.

²¹ The IRB determines if the medical record must be flagged to protect patient safety by indicating participation in the study and the source of more information on the study (IRB P&P II.2.A).

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

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 unanticipated problems involving risks to subjects or others and other reportable events²² to the IRB and the Research Service via BRAAN/CICERO according to applicable SOPs²³ and their approved DSMPs. ‘Unanticipated problems involving risks to subjects and others’ and other reportable events must be reported by the investigator to the IRB according to IRB P&P I.3.J. The IRB (through the HRPO) notifies the VAMHCS RCO when an event requiring IRB action is reported for a VAMHCS study. The IRB and the RCO report the unanticipated problem or other reportable event to the regional office of ORO and VA central office (for studies sponsored by the VA) and other regulatory and sponsoring agencies is coordinated with the HRPO in accordance with Research Service SOP 01.08, IRB P&P I.3.J, and ORO guidelines²⁴. Any proposed changes to a research study in response to an unanticipated problem or reportable event must be reviewed and approved by the IRB and VA R&D Committee before being implemented, except when necessary to eliminate apparent immediate hazards to subjects. The IRB and VA R&D Committee review and approve any report of UPRs or other events sent to regulatory or sponsoring agencies regarding a VAMHCS study.

1. Study Closure

Protocols must remain open at the IRB and the R&D Committee until data analysis is completed. 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.

Once data analysis is complete and all study-related activities have ended, the investigator must notify the IRB (through BRAAN/CICERO), the R&D Committee (through the R&D Committee coordinator) and the Chief, Pharmacy Services (through the Investigational Drug Pharmacist) (HRP 01.09).

²² See in particular, “[Conducting Human Participants Research at the VAMHCS: The Relationship of VAMHCS Research Standard Operating Procedures to the Policies and Procedures of the UMB Human Research Protections Office \(HRPO\)](#)” (HRP 01.09) and IRB P&P I.3.J.

²³ See in particular, IRB P&P I.3.J.

²⁴ Section 6 of “[Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program \(HRP 01.08\)](#), (IRB P&P I.3.J) “[Reportable Events \(Unanticipated Problems, Adverse Events, Deviations, Violations, Exceptions\)](#)”, VA Handbook 1058.1 and ORO memorandum, “[What to Report to ORO](#)” (9/8/05)

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

C. ORC Oversight of the Conduct of a Research Project

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 Research 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), “I’m a Veteran. Should I Participate in Research?” [DVA]).

The VAMHCS Research Service recognizes that data integrity is a crucial aspect of any research program. However, it also recognizes that this function is actively monitored by industry sponsors and granting agencies. The VAMHCS ORC has begun to advise investigators on implementation of their own internal data monitoring programs.²⁵

The ORC focuses its attention on matters that directly impact subject rights and safety (such as informed consent, eligibility criteria and adverse event reporting) and regulatory compliance. The Research Specialists of the Research Compliance Office conduct audits of Investigators’ study conduct on a routine or for-cause basis. Routine audits occur based on audit triggers. The ORC will respond to allegations or findings of possible mismanagement of data or noncompliance through “For-Cause” audits.

In addition, investigators are required to notify the Office of Research Compliance when they host external monitors for site visits. Monitors are now required to sign-in at the Research Service Office and, if problematic results are uncovered as a result of the visit, the ACOS/R&D, AO/R&D, or designee (the Research Compliance Officer), must attend the exit interview (see Central Research and Development Office [CRADO] memorandum, 10/14/04).

Areas of ORC review generally fall into six general categories: 1) consent process, 2) study conduct, 3) reports of unanticipated problems involving risks to participants or others, DSMB reports, DSMP conduct, 4) compliance with applicable regulations, policies and guidelines, 5) standard operating procedures and policies established by the Investigator to govern the conduct of his/her study staff, and 6) complaints and allegations of noncompliance. The results of these reviews are used for purposes of quality improvement. Remedial actions will be taken, as needed. Routine or for-cause audits specifically address categories 1-3, and generally assess categories 4 and 5.

²⁵ “Investigator Internal Quality Assurance” (HRP 02.04)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

Category 6 may initiate a for-cause audit of an Investigator and/or his/her internal policies and procedures.

Potential audit triggers are listed below:

- Routine (scheduled) spot audit
- For-cause audits
- Principal Investigator / study personnel request
- Investigator initiated studies
- Scheduled follow-up to routine audits
- PI's with high numbers of protocols
- PI's with vulnerable populations (elderly, children, psychiatric patients, persons with impaired decision-making)
- Unanticipated Problems Involving Risk to Subjects or Others or other reportable events - numerous or of interest
- Research participant/family member complaint
- Participant death
- Appearance of lack of staff support/resources/high staff turnover
- Lapses in continuing review/studies administratively closed by IRB
- Ongoing concerns about the quality of IRB or R&D Submissions
- Ongoing concerns of IRB or R&D about document processing
- ACOS/AO/R&D, Chief of Staff, MCD, RCO, Department Chair, IRB Chair, or other has concerns
- Findings of routine or other audits disclose further issues to evaluate
- Systems audits when audits, institutional reports, participant complaints or other feedback indicate that VAMHCS policies or procedures should be changed.

All active VAMHCS protocols are eligible for audit, regardless of funding source. A protocol will generally not be audited more than once unless a re-audit is recommended in the Resolution Plan or by the ACOS/R&D, the R&D Committee, or the IRB.

At the initiation of an audit, the scope of the audit is stated. Audits may be “routine” (chosen randomly for general QA) or “for-cause” (triggered by a complaint, allegation of noncompliance, or other triggers listed above). Routine and for-cause audits may be “full” (100% of research charts and documents) or “targeted” (a percentage of participants, a particular area, etc.). The procedures by which this is accomplished are described in detail in SOPs “Overview of Quality Assurance Activities” (HRP 02.01), “Audit Triggers” (HRP 02.02), “Auditing Source Documents Charts” (HRP 02.03), “Investigator Internal Quality Assurance” (HRP 02.04), and in Table 2 (“Verification of the informed Consent Process and Study Conduct”)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

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 and that no study-related procedures were initiated prior to obtaining informed consent.

The ORC 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 XII). It also offers opportunities to personally consult with the Research Compliance Officer or ORC Research Specialists, and other resources. The Informed Consent 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 I.3.F.

When copies of signed informed consent documents and HIPAA Authorizations are submitted to the Research Service to be scanned into CPRS, Research Service staff examine the documents to ensure that the correct version of the ICF has been used (IRB dates) and has been properly signed and dated (see Table 2). If these requirements are not met, the documents are returned to the Investigator for clarification.

When consent forms are scanned into CPRS, there is a check on the requirements for enrollment/consent notes.

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.

ORC Research Specialists assess the integrity of the informed consent process by using selected tools listed below (Table 2).

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

Table 2. Methods of Verification of the Informed Consent Process

Element	Method / Tool
Informed Consent Form (ICF)	
Consent form contains essential elements of informed consent and applicable additional elements of informed consent	QA Module D: Elements of Informed Consent
There is documentation that the subject or the subject's legally authorized representative has read and signed the informed consent document.	Visualization of the original and the scanned ICF; enrollment/consent note.
Consent has been obtained prior to initiating any research related procedures	Comparison between dates of ICF signatures and the date of the first research related procedure; QA Module E – Execution of ICF
Only the IRB-approved consent form has been used	Examination of the dates on the IRB approval-stamp on the ICF. Informed Consent Verification Tool or QA Module E – Execution of ICF.
The consent document has been signed and dated by the subject (or the subject's legally authorized representative), a witness, and the individual providing the information to the subject and witnesses, if applicable.	Examination of signatures; knowledge of the requirements for legal representative, witnesses and other signatures is necessary. If legal representative used, presence of documentation as to why. Pre-Scanning Check; QA Module E – Execution of ICF
The subject's medical record documents the consent process with an appropriate note and original signed consent document	Enrollment note in medical record and study binder; visualization of original form in study files.
There is documentation that the subject or the subject's legally authorized representative was provided a copy of the consent document.	Enrollment note in CPRS
There is a valid, signed HIPAA Authorization.	Informed Consent Verification Tool or Pre-scanning Check

Based on the audit reports prepared by the Research Specialists, the Research Compliance Officer evaluates the effectiveness of the consent process. This evaluation will include documentation that the following procedures have been followed:

- There is documentation the subject or the subject's legally authorized representative has read and signed the informed consent document.
- The informed consent document is signed by a witness to the signature of the subject/legal representative.
- Consent has been obtained prior to initiating any research related procedures.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- 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 and witnesses, if applicable (as well as individually initialed pages, as applicable for VA COOP studies).
- The subject’s research and medical records (CPRS) document the consent process with an appropriate note and original (or scanned into CPRS), 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.

When evaluating the informed consent process the Research Compliance Officer will give special consideration to the following populations:

- Vulnerable subjects
- Subjects likely to need surrogate consent
- Subjects participating in high risk studies.

2. Study Conduct

During the recruitment phase of a human research study, the Investigator and the research team is expected to follow the approved recruiting procedures that were submitted to BRAAN/CICERO. 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.

Table 3 Methods of Verification of Proper Conduct of the Study

Element	Method / Tool
Regulatory elements and study conduct	
Use of only IRB-approved advertisements and subject recruitment materials	Check of BRAAN Section S / CICERO
Adherence to inclusion/exclusion criteria	Audit Tool – Summary Checklists for Regulatory and Source Documents; companion tools: QA Modules B and C
Adherence to IRB approved protocols and conditions	Audit Tool – Summary Checklists for Regulatory and Source Documents;

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

	companion tools: QA Modules H and I
Obtaining IRB approval prior to initiating changes to the protocol or consent form, except where necessary to eliminate apparent immediate hazards to subjects	Audit Tool – Summary Checklists for Regulatory and Source Documents
Reporting all unanticipated problems involving risks to human subjects (including “adverse events” and deviations)	Audit Tool – Summary Checklists for Regulatory and Source Documents; companion tools: QA Module J

Based on the audit reports prepared by the Research Specialists, the Research Compliance Officer evaluates the performance of the Investigator/staff. This evaluation may include assessments of the following criteria:

- Use of only IRB-approved advertisements and subject recruitment materials.
- Adherence to inclusion/exclusion criteria
- Adherence to IRB approved protocols and conditions
- Obtaining IRB approval prior to initiating changes to the protocol or consent form, except where necessary to eliminate apparent immediate hazards to subjects
- Reporting all unanticipated problems involving risks to human subjects or others
- Reporting all protocol deviations/exceptions
- Reporting of protocol modifications
- Personnel education and training
- Credentialing of all staff

Studies with the following characteristics have the highest priority for triggering an audit:

- Investigator-initiated studies
- Investigators with numerous high-risk studies
- New investigators
- Vulnerable subjects (subjects likely to need surrogate consent, elderly, prisoners, staff/students)
- Subjects participating in high risk studies

3. Unanticipated Problems Involving Risks to Participants or Others (UPR) and Data Safety Monitoring Plan (DSMP) Conduct and Reports

The Research Service requires investigators to report adverse events and unanticipated problems involving risks to participants or others according to UMB HRPO and IRB P&P (available through the HRPO website²⁶). This is done via BRAAN/CICERO as soon as possible but within 2 working days of the investigator becoming aware of the problem.

²⁶ http://medschool.umaryland.edu/orags/hrpo/HRPP_Policies.doc

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

At the UM HRPO, reports of unanticipated problems involving risk to participants or others will initially be reviewed for appropriateness and completeness by a Quality Improvement Specialist. If the report requires immediate action before receipt of a completed report, the Quality Improvement Specialist refers the information immediately to the IRB Chair or Vice Chair on duty for the day. If the report involves a VAMHCS study, the HRPO Director of Quality Improvement or designate notifies the VAMHCS RCO. If the investigator indicates the event (1) was unforeseen, (2) caused harm or placed a person at increased risk of harm, AND (3) was related to the research procedures, the Quality Improvement Specialist places the event on the agenda of the next available IRB meeting for review. If the IRB considers the event to represent an unanticipated problem involving risks to participants or others, the matter is referred to the HRPO staff for reporting to OHRP, FDA, ORO, and sponsors according to it P&P.

The HRPO defines “Unanticipated Problems Involving Risks to Research Participants or Others (UP)” as: An event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, deaths, or other problems) that occurs any time during or after the research study, which in the opinion of the PI:

1. ***Involves harm*** to one or more participants or others, ***or placed one or more participants or others at increased risk of harm AND***
2. ***is Unexpected AND***
3. ***is Related*** to the research procedures

These include but **are not limited to**:

- A. Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:
 1. An interim analysis indicates that participants receiving investigational vaccine have a higher rate of contracting the disease than participants receiving placebo
 2. Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected
 3. A paper is published from another study that shows that an arm of your research study is of no therapeutic value
- B. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- C. Event that requires prompt reporting to the sponsor
- D. Sponsor imposed suspension for risk
- E. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
- F. Protocol violation that placed one or more participants at increased risk, or has the potential to occur again
- G. Unanticipated adverse device effect (Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)

Through regular BRAAN/CICERO access and attendance at IRB meetings, the VAMHCS Research Compliance Officer 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&D Committee, 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 ORO and VA Central Office will be in accordance with ORO guidelines as outlined in VA Handbook 1058.1 The Investigator is required to report qualified adverse events/problems to the Sponsor/coordinating center who then reports to other IRBs and external (multi-site) investigators as necessary.

The VHA defines an “Adverse Event (AE) for VAMHCS Research” as:

Any untoward occurrence (physical, psychological, social, or economic) in a human subject participating in research. An AE in research can be any unfavorable or unintended event including abnormal laboratory finding, symptom, disease, or death associated with the research or the use of as medical investigational test article. An AE in research may occur even in the absence of any error or protocol deviation and does not necessarily have to be caused by any identifiable aspect of the research.

Both UPRs and AEs for VAMHCS Research must be reported to the IRB as well as the following: adverse events that are unexpected and related to the research even if they are not serious adverse events, external adverse events which are unanticipated problems involving risk to participants or others, changes made to the research without prior IRB approval in order to eliminate apparent immediate hazard to the participants, protocol violations, protocol deviations, and protocol exceptions. [IRB P&P (I.3.J)]

Following NIH and other guidelines, the VAMHCS and the University of Maryland Human Research Protection Office have instituted Data Safety Monitoring Plans (DSMPs) for all studies on the UMB/VAMHCS campuses. At the time of protocol submission, Investigators are triggered by BRAAN/CICERO to submit a DSMP appropriate to the type of study and the risks associated with it. The structure of DSMPs is discussed in IRB P&P (III.2.D).

Investigators submit DSMP reports to the IRB according to IRB P&P. Additionally, the reports should be submitted at the time of continuing review. The Research Compliance Officer and VA R&D committee may also review these reports at the time of annual reviews. The RCO may sit on DSMBs and, as an attendee at IRB meetings, the Research Compliance Officer is instrumental in the evaluation of DSMP reports. The Research

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

Compliance Officer includes DSMP issues as part of his/her monthly reports to the R&D Committee. Follow-up occurs as needed.

4. 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. 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. Finally, in order to accept VA funding, 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.

Whether the PI's agreement is with the FDA, OHRP or VHA, 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, 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 Research Compliance Officer.

Non-compliance may come to light as a result of routine auditing, for-cause audits, routine inspection of a PI's Regulatory Documents File, or complaints or allegations from subjects or staff. The Research Compliance Officer proceeds according to the VAMHCS Research Service SOP "Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program" (HRP 01.08) and IRB P&P I.3.I, including notification of and collaboration with the UMB HRPO (through the DQI). The VA R&D committee, ACOS/R&D, COS and MCD are apprised of allegations and findings. Possible actions or penalties are outlined in the SOP. Regulatory agencies are notified according to the SOP.

The VA R&D Committee, 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. Should this occur, the investigator would be instructed to amend the protocol (remove the VAMHCS as a study site) at the IRB. The IRB could take further actions based on its policies and procedures. The RDC 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.

5. Investigator Internal Policies and Standard Operating Procedures

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

Investigators are encouraged to establish standard operating procedures within their own research programs. By establishing their own internal SOPs, “study specific” SOPs (SSSOPS)²⁷, 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 (Research Service SOP “Study Specific Standard Operating Procedures (SSSOP)” (HRP 07.06G), or institutional policies and procedures. Compliance with the Investigator’s DSMP, the informed consent process and the VAMHCS HRPP should be specifically addressed. Investigators should conduct internal quality assurance according to Research Service SOP “Investigator Internal Quality Assurance” (HRP 02.04).

The ORC and the UMB Human Research Protection Office are both actively involved in assisting Investigators to develop such programs. Both are available for consultation and provide checklists, self-assessment tools, templates for SOPs and forms, and other guidelines on their web sites or in person.

At the time of routine or for-cause audits, ORC Research Specialists will determine whether any internal standards are in effect within the Investigator’s program and whether the standards are being met. Resolution Plans may include implementation of or amendment of internal standards.

6. Complaints²⁸

The primary mechanism for research participants and research personnel to address their complaints about a research project is through contact with the VAMHCS Office of Research Compliance or the UMB IRB. The IRB-approved informed consent document includes the telephone contact information for the Principal Investigator, study staff and the IRB. 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 HRPP about their concerns.²⁹

A complainant contacts the ORC or the UMB Human Research Protections Office 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.

²⁷ 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)

²⁸ See “Addressing and Responding to Comments, Complaints and Suggestions Related to the Human Research Protection Program” (HRP 01.07)

²⁹ http://www.maryland.research.va.gov/contact_us.asp

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

If the complaint involves a veteran, a subject in a VA-approved study, research conducted on or with VA property, data or staff, the Research Compliance Officer is notified by the IRB. The Research Compliance Officer then proceeds according to VAMHCS Research Service “Addressing and Responding to Comments, Complaints and Suggestions Related to the Human Research Protection Program (HRP 01.07) (VAMHCS Policy Memorandum 512-151/RD-003). Possible actions or penalties are outlined in the SOP.

If a complaint appears to be indicative of possible noncompliance, the RCO notifies the HRPO and proceeds according to VAMHCS Research Service “Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program (HRP 01.08).

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

D. Actions & Reports

The ORC uses an assortment of tools and reporting mechanisms for its quality management process. Some of these tools are listed in Table 4. Auditors should adapt the tools to meet the specific focus of the audit.

Table 4 summarizes audit tools and reports that the ORC routinely uses:

Audit Tool	Content
Informed Consent Verification, QA Module E – Execution of ICF	Signature and date compared to IRB validation dates of ICF
QA Module D – Elements of Informed Consent	Essential elements of informed consent and applicable additional elements
Pre-scanning check, QA Module E – Execution of ICF	Signatures and dates, initials, IRB validation, HIPAA authorizations
Regulatory Chronology	Summarizes the paper trail for all regulatory requirements for the study; illustrates gaps in documentation; serves as a summary of the study’s history
Summary Checklists for Regulatory and Source Documents and associated modules	Accuracy, completeness, currentness & organization of regulatory documents file and source documents; the tool also contains ancillary tables for collecting data needed to complete the summary checklists; also associated with stand-alone “modules” to assist with data collection.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

Site Report Template	Template for executive summary and findings; Listing of deficiencies and progress of resolution
Investigator Interview Checklist	Report of many aspects of an investigator's research program based on interviews
Pharmacy Audit Tools:	
Study Subject Worksheet	Looks for audit elements in individual subject charts.
Form A: Investigational Drug Dispensing Tool	Looks for regulatory documents for in the pharmacy chart.
Form B: Investigational Drug Log Tool	Looks for specific elements on the drug log sheet and in the drug dispensing documentation.
Form C: Investigational Pharmacy Audit Report	Summarizes audit findings.

The Research Compliance Officer's evaluation of any of the reports generated by the QMP may result in any of the following actions:

- The Research Compliance Officer finds that an Investigator is in compliance with internal, institutional and regulatory requirements.
- The Research Compliance Officer finds general compliance with internal, institutional and regulatory requirements but finds that some action is required in order to be in full compliance. The Research Compliance Officer/staff works with the Investigator/staff to develop corrective policies and procedures and re-evaluates the Investigator at least once within the following year to ensure that corrective actions have been implemented.
- The Research Compliance Officer finds significant deficiencies in the Investigator's/staff's processes that place research subjects at risk. The RCO immediately notifies the ACOS for Research, the COS, the MCD, Chair of the VAMHCS RDC, and the UMB IRB. After a review of the situation, the MCD, the convened RDC, the IRB chair, or convened IRB will take the necessary corrective action which may include suspension of new enrollment, and study termination (see UMB P&P I.3.I and HRP 01.08). More detailed, for-cause audits and/or intensive consultations between the Research Compliance Office, UMB IRB, the RDC and the Investigator may be necessary in order to resolve issues.
- The Research Compliance Officer discovers systemic deficiencies within institutional policies and procedures. These deficiencies will be brought to the attention of the ACOS for R&D, the R&D Committee, the COS and MCD. 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. Once the new policies and procedures are approved by the ACOS for R&D and, if applicable, the Medical Director or the HRPO, the ORC notifies research practitioners, implements the

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

policy/procedure, and evaluates the new policy/procedure after an appropriate interval.

The Research Compliance Officer reports to Institutional agents according to the following table:

Person / Committee	Minimum Frequency	Content
ACOS/AO for R&D	Weekly	Issues, DSMP minutes, QA reports & IRB minutes, ICV and JCAHO ICF audits
Chief of Staff	Biweekly	
R&D Committee	Monthly	
MCD	Monthly	Ongoing compliance issues, audits, follow-ups on complaints, etc.
VISN leadership	Monthly	Ongoing compliance issues, audits, follow-ups on complaints, etc.
EPIC	Quarterly	QA reports
HRPOC	Biweekly-monthly	Issues, policy reviews
IRB	Weekly	Ongoing compliance issues, audits, follow-ups on complaints, etc.

VIII. Quality Management Plan: Investigational Drug Service³⁰

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 Research Compliance Office, and investigators.

The VAMHCS Investigational Drug Service Pharmacist (IDP) and the Research Compliance Officer 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

³⁰ References and applicable policy memoranda are located in Section XIII: 11, 19, 23, 29, 38, 45.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

develop resolution plans, and to comply with JCAHO and AAHRPP standards. The IDP sits on the Human Research Protections Oversight and Compliance Subcommittee (HRPOC) and other R&D Committee subcommittees as a formalized way to accomplish this.

The IDP also sits on the VAMHCS R&D Committee 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 significant 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&D Committee, they are required to include a “Research Methods Accountability Form” if the protocol involves the use of any study drug/placebo, or a device to be controlled by the Investigational Pharmacy. They must also submit an “Attestation for the Use of Devices”, an “Attestation for the Use of Equipment in the Conduct of a Research Study”, and/or an “Attestation for the Performance of Procedures in the Conduct of a Research Study” if the protocol involves the use of any research-related device, equipment or procedure, whether investigational or not.³¹

In most cases, study drugs are dispensed through the IDS. However in some very unique cases, it is possible for study drugs to be dispensed by investigators themselves. These plans must undergo extensive review and approval by the IDP and the Chief, Pharmacy Service before they can be submitted to the R&D Committee³². If such a plan is approved, the investigator must keep all records specified below and must report regularly to the IDS. The Investigator is also open to audits by the ORC.

Plans for the control of study devices are approved by the UMB IRB and VA R&D committee. In most cases, study devices are managed by the investigators or their staffs. However the IDS may also be designated to manage investigational devices. Investigators must attest to their understanding of VAMHCS policies and the qualifications of their staffs and agree to proper documentation in order to have the study approved. This is done via the “Attestation for the Use of Devices” form which is submitted with the R&D submission documents.

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 BRAAN/CICERO:

- A copy of the approved protocol
- A copy of the current, approved ICF

³¹ See the following SOPs:

HRP 05.01: “Research and Investigational Drugs”

HRP 06.01: “Accountability for the Use of Devices and Procedures in the Conduct of Research”

³² See VAMHCS SOP 119-010 “Investigational Drug Section”.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

- IRB approval letter
- VA Form 10-1223
- R&D approval letter
- Page 2 of the Research Methods Accountability Form
- 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 BRAAN/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
- 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 Research Specialists of the Research Compliance Office conduct audits of the Investigational Pharmacy on a routine or for-cause basis. The audit includes:

- Presence (or access through BRAAN/CICERO) of approved protocol, approval letters (including 10-1223), signed ICFs and 10-9012
- Records of storage and security of investigational drug supply
- Records of receipt and dispensing of investigational drug supply

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

- 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)
- Research & Investigational Drugs (HRP 05.01)
- Accountability for the Use of Devices and Procedures in the Conduct of Research Studies (HRP 06.01)

The Research Compliance Officer's evaluation of the Investigational Pharmacy may result in any of the following actions:

- The Research Compliance Officer finds that the Investigational Pharmacist is in compliance with internal, institutional and regulatory requirements for compliance and documentation.
- The Research Compliance Officer 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 Research Compliance Officer/staff works with the Investigational Pharmacist to develop corrective policies and procedures.
- The Research Compliance Officer finds significant deficiencies in the Investigational Pharmacist's compliance and documentation and immediately notifies the ACOS for Research and the UMB IRB. If necessary, VAMHCS stud(ies) are suspended until corrective actions are in effect. More detailed, for-cause audits and/or intensive consultations between the Research Compliance Office and the Pharmacy Service may be necessary in order to formulate remedial actions.
- The Research Compliance Officer discovers systemic deficiencies within institutional policies and procedures. See actions discussed above. Once the new policies and procedures are approved by the ACOS for R&D and, if applicable, the Medical Director, the RC Office notifies/educates the research practitioners, implements the P&P, and evaluates the new P&P after an appropriate interval.

IX. Quality Management Plan: 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

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

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 about research ethics and human subject protection,
2. specific knowledge about the VAMHCS HRPP/QMP, and
3. continual or periodic updates on changes in the HRPP/QMP, VA regulations, federal and state regulations, UMB IRB policies and procedures, and other institutional changes.

A summary of educational requirements is available in Table 5.

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.³³ WOCs must also submit documentation of their Scope of Practice for involvement in a protocol and their qualifications to perform those study activities. In addition, all members of the R&D Committee and the Human Research Protections Oversight and Compliance Subcommittee must complete the education and training requirements listed below.

The VA Research Service will maintain tracking systems to confirm that individuals in the above categories (investigators, research staff, committee and subcommittee members, etc.) have completed the VA training requirements.

Separate spreadsheets will be maintained for committee/subcommittee members and investigators/research staff. In general, all staff are responsible for maintaining their own requirements/certifications. However, if Research Service staffing allows, personnel will be reminded as their time for renewal of requirements approaches. No protocol will be accepted for review by the VAMHCS R&D Committee if the investigator(s) and their research staff’s VA training requirements are not up to date. As part of submissions of protocols to the R&D Committee, PIs must provide training certificates for themselves, their co-investigators and staff.

It is also recognized that Quality Management Plan 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 about research ethics and human subject protection

All individuals who are involved in human studies research will receive appropriate training in the ethical principles and accepted practices on which human studies research should be conducted. VAMCS investigators and research staff must provide documentation for the following requirements:

³³ See SOPs 04.01 “Research Personnel Training” and 04.03 “Research Personnel Employment – WOC”

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- a. completion of appropriate level of basic education
- b. completion of appropriate level of professional training
- c. valid licensure and /or certifications (credentialing)
- d. Annual combined training in Good Clinical Practices (GCP) and Collaborative IRB Training Initiatives (CITI) is available via web-based training at www.citiprogram.org.
- e. Annual VA Privacy Policy training (HIPAA training specific to the VA). See the Research Service training/education webpage³⁴ for current information on access.
- f. Annual Cybersecurity training (for staff with VAMHCS computer access). See the Research Service training/education webpage for current information on access.
- g. Annual VA Research Data Security & Privacy training. See the Research Service training/education webpage for current information on access.

Principle investigators must provide proof of completion of required training for themselves and their staff in order to submit protocols to the R&D Committee for approval. A database (VetPro) and an Excel spreadsheet kept in the Research Service Office track these requirements and are updated by Research Service Staff.

Additional information can be found in the Research 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. Research Service website: www.maryland.research.va.gov.
 - b. Research Service Hot Topics series: http://www.maryland.research.va.gov/hot_topics.asp
 - c. Email broadcasts to investigators and research staff
 - d. Investigator/staff education sessions
Past topics include: CPRS Clinical Warning, VAMHCS GCP requirements
Proposed topics include: Advanced GCPs, Research Nurse Liaisons
 - e. Education designed to improve adherence to the HRPP
 - f. Other mandatory investigator meetings (Ex: HIPAA, BRAAN/CICERO)
 - g. Manuals
 - h. HRPO education sessions
 - i. VAMHCS Nurse Orientation
 - 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

³⁴ http://www.maryland.research.va.gov/training/human_subject_trng.asp

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

- b. Email broadcasts to investigators and research staff
- c. Individual/group trainings/consultations as requested
- d. ACRP monthly chapter meetings (Baltimore-Chesapeake Bay Chapter)
- e. Continuing education activities offered by research-related professional organizations such as ACRP, PRIM&R, ARENA, AAHRPP, etc.

Table 5. VAMHCS HRPP Education and Training Requirements

Requirement	Verification
Completion of appropriate level of basic education	College transcript, Post-graduate transcript(s)
Completion of appropriate level of professional training	Transcripts from professional schools (medical, nursing, graduate); VetPro/RNs
Valid licensure and /or certifications	Current license and/or certification; VetPro
Annual training in Good Clinical Practices	Certificate of attendance/completion; Research Service Excel spreadsheet updated as certifications are submitted
Annual training in Human Subjects Protection	Certificate of completion (CITI); Research Service Excel spreadsheet updated as certifications are submitted
Annual HIPAA training specific to the VAMHCS	Attendance sheets / certificates; Research Service Excel spreadsheet updated as certifications are submitted
Mandatory investigator/research staff training sessions	Attendance sheets / certificates
Mandatory investigator/research staff broadcasts	Email responses
Continuing education	Certificates of attendance

Hospital-wide Clinical Staff

Safe conduct of studies often depends on the general clinical staff's understanding of research protocols and investigational agents. Hospital wide medical care staff is educated through DHCP broadcasts, inservices, grand rounds, etc. Past topics have included: identifying research subjects via the CPRS electronic database, Clinical Warnings/drug information, importance of precise study drug administration, and understanding the need to notify study staff when appropriate (e.g., deaths, VAMHCS hospital admissions, ER visits, and clinic visits of significance).

During the hospital's orientation of new staff, the Research Compliance Officer gives a talk on research activities at the VAMHCS and the roles that hospital staff may be asked

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

to serve for research studies such as administering study medications, documenting study events, and performing study activities.

X Quality Management Plan: Program Oversight

The oversight of the VAMHCS Human Research Protections Program rests with two bodies: the R&D Committee and the Office of Research Compliance. The Chair of the R&D Committee and the Research Compliance Officer (RCO) (director of the Office of Research Compliance) answer, through the Chief of Staff, to the VAMHCS Medical Center Director. They therefore act independently of the ACOS/R&D.

The role of the R&D Committee in this respect is summarized in section IV.C.8 of this document and in more detail in HRP 01.03 “Research & Development Committee”. The role of the RCO is summarized in section IV.C.6 of this document and described in detail in many of the Research Service SOPs.

In addition, the Research Service routinely evaluates the effectiveness of the IRB through review of IRB minutes at R&D Committee meetings, attendance of ORC staff as observers at IRB meetings, and audits of IRB functions.

In compliance with VHA Handbook 1200.1, the R&D Committee annually reviews resources allocated to the Human research Protections Program and presents recommendations to the MCD and ACOS/R&D. In addition, as part of the ongoing QMP, the Office of Research Compliance audits all aspects of the program. 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&D Committee reviews the quality and effectiveness of the IRB, and the VAMHCS Human Research Protections Program. 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 R&D Committee (via the HRPOC) and the Medical Center Director and shared with the Executive Performance Improvement Committee. Collaboration with the UMB HRPO and the UMB ORC shall be maintained to ensure harmonization of quality management activities for human research being conducted at the VAMHCS and UMMS.

VAMHCS HUMAN RESEARCH PROTECTION PLAN (HRP 01.02)

XI Long Term Approach

The Human Research Protection Plan presented here is comprised of many elements: standard operating procedures & guidelines, education & training, reports & problem solving, and the committees, staff and officials who are committed to the goal of safe, ethical and productive clinical research. It is built on a wealth of experience with VAMHCS programs that have worked, with problems that have spurred analysis and improvements, and with adaptation to changing regulations and other external requirements.

The VAMHCS is committed to this process of continual assessment and improvement of the HRPP. A comparison of prior versions of the HRPP is a good example of this.

Since the 2006-2007 version, the following goals of that HRPP have been acted upon:

- an increase in audit activities in order to identify systemic problem areas,
- launch of the Research Service website,
- self-assessment for AAHRPP accreditation (ongoing),
- development of VA-specific content and workflow in the new IRB electronic protocol management system, “CICERO” (ongoing),
- inclusion of VA-specific items in the UMB IRB SOPs and reviewer checklists,
- a research participants’ satisfaction survey project, and
- institution of the “Research Service Hot Topics” series.

In addition, new VACO initiatives in the review and oversight of cyber security, data security and privacy were implemented in response to VA ORD mandates, directives and policies (<http://www.research.va.gov/resources/data-security/policies.cfm>). These initiatives required changes in the investigator application for VAMHCS R&D Committee protocol review.

In the coming year we plan to further improve our HRPP by acting on the following goals:

- Prepare for AAHRPP accreditation,
- increase our audit activities in order to identify systemic problem areas,
- continue working with the UMB IRB on CICERO in order to fine-tune it to best reflect VA needs,
- formalize outreach to research subjects in order to assess their level of satisfaction with their VAMHCS research experience and potential opportunities for improvement,
- maintain the number of routine audits of study files per year,
- increase training and education activities, including updates on standard operating procedures and other VAMHCS-specific and IRB-specific changes
- increase outreach and education about research to hospital staff.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

XII Quality Management Program: Guidelines and Resources for Investigators and Staff

A. Campus Websites

1. Research Service Website
www.maryland.research.va.gov
2. UMB Human Research Protections Office website
<http://medschool.umaryland.edu/ORAGS/hrpo/policies.asp>

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 Research Service website, www.maryland.research.va.gov, or through the Research Service Office (3-A-125),

9. "VA Human Studies Approval Requirements" (VA R&D Checklist; available in the Research Service office)
10. Audit Tool – Summary Checklists for Regulatory and Source Documents
11. Regulatory Chronology
12. Module A – Staff Requirements
13. Module B – Entry Criteria (individual subjects)
14. Module C – Lab Inclusion-Exclusion
15. Module D – Elements of Informed Consent Forms
16. Module E – Execution of Informed Consent Form
17. Module F – Execution of HIPAA
18. Module G – Informed Consent Process
19. Module H – Source Documents Audit
20. Module I – Research Procedures
21. Module J – Unanticipated Events (AEs)
22. Pre-Audit Investigator Interview Checklist
23. Clinical Trial Standards That *May* Be Applied During Audit Proceedings
24. Documents Subject to Audits
25. Essential and Additional Elements of Informed Consent
26. Lay Language for Informed Consent
27. Tests of Understanding and Decisional Capacity

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

28. Informed Consent Process Worksheet
29. Sample credentialing/training log
30. Sample Accountability log
31. Enrollment Note Form
32. Clinical Warning Form
33. Sample Clinical Warning
34. Guidelines for Time-Event Sheets
35. Examples of Time-Event Sheets
36. CRF-DCF Template
37. Guidelines for Narrative Notes
38. Template of standard operating procedure (SOP) format
39. Cover letter for Scanning of Informed Consent Forms
40. Pre-Study Assignment of Responsibilities – Sponsor
41. Pre-Study Assignment of Responsibilities – Staff
42. Self-Assessment – Investigator Interview Checklist
43. Self-Assessment – Investigator Records Checklist
44. Self-Assessment – Subject Records Checklist
45. Complaint Information Form
46. “I’m a Veteran. Should I Participate in Research?” (pamphlet produced by the Department of Veterans Affairs, available in the Office of Research Compliance)

D. Selected Forms

47. Attestation for the Use of Devices
48. Attestation for the Use of Equipment in the Conduct of a Research Study
49. Attestation for the Performance of Procedures in the Conduct of a Research Study
50. Research Methods Accountability Form (RMAF) (available in the Research Service office)
51. Clinical Trials Data Sheet (available in the Research Service office)
52. Investigational Drug Information Record – VA Form 10-9012 (available in the Research Service office)
53. VA Pharmacy Use Initiation Forms (available in the Research Service office)
54. Data Security Checklist for Principal Investigators

E. Research Service Standard Operating Procedures

55. Research & Development Committee (HRP 01.03)
56. Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program (HRP 01.07)
57. Conducting Human Participants Research at the VAMHCS: The Relationship of VAMHCS Research Standard Operating Procedures to the Policies and

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

Procedures of the UMB Human Research Protections Office (HRPO) (HRP 01.08)

58. Conducting Human Participants Research at the VAMHCS: The Relationship of VAMHCS Standard Operating Procedures to the Policies & Procedures of the UMB Human Research Protections Office (HRPO) (HRP 01.09)
59. Review of Research Documentation for Compliance with Privacy Requirements (HRP 01.12)
60. Information Security Review of Research Protocols (HRP 01.13)
61. Overview of Quality Assurance Activities (HRP 02.01)
62. Audit Triggers (HRP 02.02)
63. Auditing Source Documents Charts (HRP 02.03)
64. Investigator Internal Quality Assurance (HRP 02.04)
65. Auditing the Investigational Pharmacy (HRP 02.05)
66. Writing a VAMHCS Informed Consent Form (HRP 03.02)
67. Obtaining and Documenting Informed Consent (HRP 03.03)
68. Research Personnel Training (HRP 04.02)
69. Research Personnel Employment –WOC (HRP 04.03)
70. Research & Investigational Drugs (HRP 05.01)
71. Accountability for the Use of Devices and Procedures in the Conduct of Research Studies (HRP 06.01)
72. “Enrollment Notes for Research Participants” (07.01)

F. UMB

73. UMB policies and tools are available at the website,
<http://medschool.umaryland.edu/ORAGS/hrpo/policies.asp>

G. Federal Sources

74. VHA Handbook (1200.1), “Research and Development Committee”
75. VHA Handbook (1200.5), “Requirements for the Protection of Human Subjects in Research”
76. VHA Handbook (1108.04), “Investigational Drugs and Supplies”
77. VHA Handbook (1058.1), “Reporting Adverse Events in Research to the Office of research Oversight”
78. VHA Handbook (1605.1), “Privacy and release of Information”
79. 45 CFR 46 (DHHS)
80. 38 CFR 16 (VA)
81. 38 CFR 17 (VA)
82. ORO Memorandum, “What to Report to ORO” (9/8/05)

H. Other

83. Belmont Report
84. Declaration of Helsinki
85. ICH Guidelines
86. CITI (www.citiprogram.org.)

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

87. LMS website
88. AAHRPP Evaluation Instrument for Accreditation for VA Facilities and Academic Affiliates

XIII 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 (1200.1), “Research and Development Committee”
8. VHA Handbook (1200.5), “Requirements for the Protection of Human Subjects in Research”
9. VHA Handbook 1605.1, “Privacy and Release of Information”
10. VHA Handbook 1605.2 “Minimum Necessary Standard for Protected Health Information”
11. VHA Handbook 1108.4, “Investigational Drugs”
12. VHA Handbook 1058, “Research Misconduct”
13. Central Research and Development Office (CRADO) memorandum (10/14/04), “Reporting of All Study Site-Monitoring Visit Results”
14. <http://www1.va.gov/oro/docs/Facility-Director-Cert-Checklist-032307.doc>
15. ORO Memorandum, “What to Report to ORO” (9/8/05)

C. VAMHCS Sources

16. FWA – VAMHCS
17. FWA – BREF
18. MOU – IRB
19. The Human Research Protection Program (HRPP) (HRP 01.01) (VAMHCS Policy Memorandum 512-151/RD-004)
20. Conducting Human Participants Research at the VAMHCS: The Relationship of VAMHCS Research Standard Operating Procedures to the Policies and Procedures of the UMB Human Research Protections Office (HRPO) (HRP 01.09)
21. Establishment of a Human Research Protection Program Committee (HRP 01.05)
22. Overview of Quality Assurance Activities (HRP 02.01)
23. Research and Development Committee (HRP 01.03)
24. Establishment of the Human Research Protection Program Committee (HRP 01.06)
25. “Executive Performance Improvement Council (EPIC)”, VAMHCS Policy Memorandum 512-14/A&PI-100
26. “Performance Improvement Program”, VAMHCS Policy Memorandum 512-14/PI-03

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

27. “Patient Safety/Risk Management Program”, VAMHCS Policy Memorandum 512-14/RM-05
 28. Job descriptions on file in the Research Service Office
 29. Research and Investigational Drugs (HRP 05.01)
 30. Review of Research Documentation for Compliance with Privacy Requirements (HRP 01.12)
 31. Information Security Review of Research Protocols (HRP 01.13)
 32. Negotiating and Entering into a Phase I, II, III, and IV Clinical Trials Agreements (CTA) with Sponsors (HRP 01.14)
 33. Negotiating and Entering into a Phase I, II, III, and IV Clinical Trial Cooperative Research and Development Agreements (CRADA) (HRP 01.15)
 34. Addressing and Responding to Comments, Complaints and Suggestions Related to the Human Research Protection Program (HRP 01.07)
 35. Addressing and Responding to Allegations of Noncompliance with Institutional Policies Related to the Human Research Protection Program (HRP 01.08)
 36. Audit Triggers (HRP 02.02)
 37. Auditing Source Documents Charts (HRP 02.03)
 38. Auditing the Investigational Pharmacy (HRP 02.05)
 39. “Sentinel Event/Root Cause Analysis”, VAMHCS Policy Memorandum 512-14/RM-02
 40. Informed Consent Guidebook (HRP 03.01G)
 41. Writing a VAMHCS Informed Consent Form (HRP 03.02)
 42. Obtaining and Documenting Informed Consent (HRP 03.03)
 43. Research Personnel Training (HRP 04.02)
 44. Research Personnel Employment – WOC (HRP 04.03)
 45. Accountability for the Use of Devices and Procedures in the Conduct of Research Studies (HRP 06.01)
 46. Enrollment Notes for Research Participants (HRP 07.01)
 47. Guidelines for Setting Up a Study Binder and Regulatory Documents Binder (HRP 07.02G)
 48. Guidance on Source Documents (HRP 07.03G)
 49. “I’m a Veteran. Should I Participate in Research?” (pamphlet produced by the Department of Veterans Affairs)
 50. Investigator Internal QA (HRP 02.04)
 51. Study-Specific Standard Operating Procedures (SSSOPs) (HRP07.06G)
- D. UMB Sources
52. FWA – UMB
 53. HRPO and IRB Policies and Procedures;
<https://medschool.umaryland.edu/hrpo/policies.asp>
 54. IRB Reviewer Checklists;
<https://medschool.umaryland.edu/ORAGS/hrpo/irbchecklists.asp>
- E. External Sources
55. The Belmont Report
 56. International Conference on Harmonization (ICH) E6, Good Clinical Practice

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

: Consolidated Guideline

57. AAHRPP Evaluation Instrument for Accreditation for VA Facilities and Academic Affiliates; <http://www.aahrpp.org/www.aspx?PageID=95>

XIV. Attachments (follow)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

ATTACHMENT 1:

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

Attachment 1 is available in the Research Office.

ATTACHMENT 2:

Flowchart of the Implementation of the VAMHCS HRPP

Attachment 2 is available in the Research Office.

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

ATTACHMENT 3: VAMHCS FWA

ASSURANCE: FWA00001483 - VA Maryland Hlth Care

System

Located at: Baltimore, MARYLAND

Expires: October 9, 2010

COMPONENTS IDENTIFIED FOR THIS ASSURANCE				
Name	City	State or Country		
Baltimore VAMC	BATIMORE	MARYLAND		
Baltimore Vet Center	BALTIMORE	MARYLAND		
Cambridge Outpatient Clinic	CAMBRIDGE	MARYLAND		
Cambridge Vet Center	CAMBRIDGE	MARYLAND		
Elkton Vet Center	ELKTON	MARYLAND		
Glen Burnie Outpatient Clinic	GLEN BURNIE	MARYLAND		
Loch Raven VA Outpatient Cln	BALTIMORE	MARYLAND		
Loch Raven VAMC	Baltimore	MARYLAND		
Perry Point VAMC	PERRY POINT	MARYLAND		
Pocomoke City Outpatient Clinic	POCOMOKE	MARYLAND		
Silver Spring Vet Center	SILVER SPRING	MARYLAND		
Southern Maryland VA Outpatient Clinic	CHARLOTTE HALL	MARYLAND		
VA Medical Center	PERRY POINT	MARYLAND		
VA Outpatient Clinic	FORT HOWARD	MARYLAND		
IRBS LINKED TO THIS ASSURANCE				
Ident	Name	City	State or Country	
IRB00000233	U of Maryland, Baltimore, Professional Schools IRB #1	Baltimore	MARYLAND	Detail
IRB00000234	U of Maryland, Baltimore, Professional Schools IRB #2	Baltimore	MARYLAND	Detail
IRB00000235	U of Maryland, Baltimore, Professional Schools IRB #3	Baltimore	MARYLAND	Detail

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

IRB00002923	U of Maryland, Baltimore, Professional Schools IRB #4	Baltimore	MARYLAND	Detail
IRB00006045	U of Maryland, Baltimore, Professional Schools IRB #5	Baltimore	MARYLAND	Detail

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

ATTACHMENT 4: BREF FWA

ASSURANCE: FWA00001420 - Baltimore Rsch & Educ

Fdn

Located at: Baltimore, MARYLAND

Expires: August 24, 2010

No Assurance Components Identified

IRBS LINKED TO THIS ASSURANCE				
Ident	Name	City	State or Country	
IRB00000233	U of Maryland, Baltimore, Professional Schools IRB #1	Baltimore	MARYLAND	Detail
IRB00000234	U of Maryland, Baltimore, Professional Schools IRB #2	Baltimore	MARYLAND	Detail
IRB00000235	U of Maryland, Baltimore, Professional Schools IRB #3	Baltimore	MARYLAND	Detail
IRB00002923	U of Maryland, Baltimore, Professional Schools IRB #4	Baltimore	MARYLAND	Detail
IRB00006045	U of Maryland, Baltimore, Professional Schools IRB #5	Baltimore	MARYLAND	Detail

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

ATTACHMENT 5: UMB FWA

ASSURANCE INFORMATION
ASSURANCE: fwa00007145 - U of Maryland, Baltimore, Professional Schools
NEW SEARCH
Schools
Located at: Baltimore, MARYLAND
Expires: June 28, 2010
COMPONENTS IDENTIFIED FOR THIS ASSURANCE

Name	City	State or Country
Kernan Hosp	Baltimore	MARYLAND
Maryland Psychiatric Rsch Ctr	Catsonville	MARYLAND
U of Maryland School of Dentistry	Baltimore	MARYLAND
U of Maryland School of Law	Baltimore	MARYLAND
U of Maryland School of Medicine	Baltimore	MARYLAND
U of Maryland School of Nursing	Baltimore	MARYLAND
U of Maryland School of Pharmacy	Baltimore	MARYLAND
U of Maryland School of Public Health	Baltimore	MARYLAND
U of Maryland School of Social Work	Baltimore	MARYLAND

IRBS LINKED TO THIS ASSURANCE

Ident	Name	City	State or Country	
IRB00000233	U of Maryland, Baltimore, Professional Schools IRB #1	Baltimore	MARYLAND	Detail
IRB00000234	U of Maryland, Baltimore, Professional Schools IRB #2	Baltimore	MARYLAND	Detail
IRB00000235	U of Maryland, Baltimore, Professional Schools IRB #3	Baltimore	MARYLAND	Detail
IRB00002923	U of Maryland, Baltimore, Professional Schools IRB #4	Baltimore	MARYLAND	Detail
IRB00006045	U of Maryland, Baltimore, Professional Schools IRB #5	Baltimore	MARYLAND	Detail

[Agency Only Access](#)

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

**ATTACHMENT 6: Memorandum of Understanding
between
University of Maryland School of Medicine
and
VA Maryland Health Care System
and
Baltimore Research and Education Foundation, Inc.**

**Concerning the Use of the University Registered Assurance FWA #
00007145**

Purpose

This Memorandum of Understanding (“MOU”) sets forth the agreement between the University of Maryland School of Medicine (“University” or “School”), the VA Maryland Health Care System (“VAMHCS”), which is part of the United States Department of Veterans Affairs (“VA”), and the Baltimore Research and Education Foundation, Inc. (“BREF”), concerning the use of the University’s Registered IRB numbers 00000233, 00000234, 00000235, 00002923 and 00006045 under the auspices of the Federal Wide Assurance (“FWA”) assigned by the Office for Human Research Protections (“OHRP”), to the University (FWA # 00007145), the VAMHCS (FWA # 00001483) and BREF (FWA # 00001420).

The University’s Institutional Review Board (“University IRBs”) will serve as the IRBs of record for review and approval of all human subjects research protocols proposed by Principle Investigators with joint VAMHCS/University appointments, conducted at the VAMHCS and/or funded by the Department of Veterans Affairs and/or through the BREF. The University IRBs will be responsible for independent review and approval of all VAMHCS/BREF human subjects research protocols including, but not limited to, initial protocol review, amendment review, continuing review, exemption determinations and all other aspects of review, approval and assurance of compliance with all human research protection policies and procedures. The VAMHCS and BREF will be responsible for assuring that each VAMHCS/BREF human subjects research protocol is reviewed and approved by one of the University IRBs and subsequently by the VAMHCS Research and Development Committee (“VAMHCS R&D Committee”) prior to initiation of the protocol. In its review of human use protocols the VAMHCS R&D Committee may disapprove protocols approved by a University IRBs, but may not approve any protocol not approved by a University IRBs.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

The University, the VAMHCS and BREF will base their policies and procedures on high ethical standards and will collaborate to ensure that policies and procedures are complementary between the institutions. These policies and procedures govern the working relationship of the institutions (University, VAMHCS and BREF) with research participants, investigators and staff, sponsors, and one another.

The University, VAMHCS, and BREF agree to each of the following provisions:

Article 1. General Procedures:

1.1. The University, the VAMHCS and BREF each has a FWA. Each agrees to abide by all applicable federal, state and local laws and policies in the conduct of human subjects research at its facilities and in its programs, and specifically agrees to follow the Federal Policy for Human Subject Protections (“the Common Rule”), 45 CFR §46 Subparts A through D and 38 CFR §16, §17, and, where applicable 21 CFR §50 and §56, other pertinent federal laws and guidance, and VA policies, including, but not limited to Veterans Health Administration (“VHA”) Handbook 1200.5. VAMHCS will only use as its IRB of record an IRB of an entity that has an active FWA. VAMHCS will not enter into any collaboration with any institution that does not have a FWA.

1.2. The VAMHCS Research & Development Service will:

- a. Provide initial and ongoing training for VAMHCS and BREF FWA signatory officials, for all members of the VAMHCS Research & Development Committee, and for physicians, scientists, other health care workers and other research personnel participating in human subjects research at VAMHCS facilities or under VAMHCS or BREF sponsorship, or research involving recruitment of VAMHCS subjects for study participation (all such research, collectively, being referred to in this MOU as “VAMHCS Human Subjects Research”). Participation in such training shall be required for all members of the VAMHCS R&D Committee and for VAMHCS representatives appointed to the University IRBs.
- b. Provide access and training to the University IRBs regarding VAMHCS policies and procedures that govern the VA Maryland Health Care System Human Research Protection Program (“VAMHCS HRPP”) processes and determinations.
- c. Provide access to research subjects' clinical records and/or case file to the University IRBs and the UMB Human Research Protection Program (“University HRPP”) as required for monitoring research activity to the extent permitted by law. This includes any University IRBs member or designate and the head of the University Human Research Protections Office (“University HRPO”) or designate.
- d. Assure that the VAMHCS R&D Committee considers the University IRBs review, and provides approval prior to the conduct of covered VAMHCS Human Subjects Research. VAMHCS Research Service will work with the

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

University to develop mutually acceptable policies for monitoring human research, and for providing regular communication of results of this monitoring, and other documentation of VAMHCS Human Subjects Research to the VAMHCS R&D Committee. The University will provide information monthly including University IRBs minutes, correspondence, and reports of quality improvement activities to the VAMHCS R&D Committee. VAMHCS Research Service will provide information to the University IRBs about significant issues that come to light in the VAMHCS approval process that might affect the conduct of a protocol.

- e. Maintain current written Standard Operating Procedures (“SOP”) that incorporate procedures for reviewing and approving VAMHCS Human Subjects Research.
- f. Promptly inform the University IRBs of any problems, including complaints, and serious/unanticipated events, encountered in VAMHCS Human Subjects Research as detailed in VAMHCS SOPs 01.07 “complaints” and 01.08 “allegations of noncompliance”.
- g. Nominate representatives to each University IRBs that reviews VAMHCS Human Subjects Research. At least two members (and alternates when possible) must be appointed to each University IRBs panel that is a University IRBs of record for VAMHCS Human Subjects Research.
 - Members who are VAMHCS representatives must be VAMHCS salaried for at least 5/8 FTEE.
 - At least one VAMHCS representative member must have scientific expertise.
 - The VAMHCS representatives must be full voting members of the University IRBs (i.e., they will participate in review of all protocols, not just VAMHCS protocols).
 - A VAMHCS voting member must be present during full board review of VAMHCS Human Subjects Research.
- h. Promptly notify the University IRBs of any modifications to the VAMHCS and/or BREF FWA or changes to the status of the Assurance documents.
- i. Develop SOPs that detail how compliance monitoring, audits, and reporting to appropriate regulatory authorities will be handled by administrative officials, research compliance officer, and the University IRBs and its administrators.
- j. Instruct its investigators and staff that University HRPO policies and procedures apply to VAMHCS research staff except where explicitly stated in the policies and procedures.
- k. Provide the results of any external monitoring or audits of human subjects research activity to the University IRBs including visits by sponsors and regulatory/compliance bodies.
- l. Actively cooperate with the University in both VAMHCS and University

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

HRPP in resolving any problems encountered in either program. Should problems become irresolvable, either party may terminate this MOU as provided below.

- m. Assure that all key VAMHCS personnel engaged in research meet both VAMHCS and University IRBs training requirements and that there is a tracking system.
- n. Make available to the University the required annual VAMHCS review and evaluation of the University IRBs structure, function and performance as completed by the VAMHCS R&D Committee for the VAMHCS Institutional Official.
- o. Provide and facilitate the use of the VA Form 10-1086 by the University.
- p. Assure that no human research will be conducted at VAMHCS or by its personnel without University IRBs approval or University IRBs determination that the activity is exempt from review.
- q. Assure that VAMHCS R&D Committee approval is obtained after IRB approval and before VAMHC Human Subject Research is initiated.
- r. Assure that the VAMHCS R&D Committee does not approve any project that the University IRBs has not approved.
- s. Assure that VAMHCS Human Subjects Research is conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA).
- t. Notify the University IRB of any potential institutional conflicts of interest.
- u. Adhere to requirements of affiliate regarding reporting Conflict of Interest for University IRBs members.

1.3. The University will:

- a. Provide access or provide requisite information from the University IRBs database to approved representatives of the VAMHCS Research Service for the purposes tracking ongoing VAMHCS Human Subjects Research activity.
- b. Develop mutually acceptable policies for monitoring VAMHCS Human Subjects Research, and for monthly communication of results of this monitoring, and other documentation of VAMHCS Human Subjects Research to the VAMHCS R&D Committee.
- c. Monthly, provide information including minutes, correspondence, and reports of quality improvement activities to the VAMHCS R&D Committee.
- d. Provide training to VAMHCS staff and investigators as appropriate for compliance with University IRBs policies and submission procedures as they apply to VAMHCS submissions.
- e. Maintain University IRBs policies and procedures that incorporate, either by inclusion or reference, VAMHCS policies and procedures applicable to reviewing VAMHCS Human Subjects Research.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- f. Promptly inform the VAMHCS Research Service of any issues or complaints associated with VAMHCS Human Subjects Research. This includes serious/unanticipated adverse event reports observed in VAMHCS Human Subjects Research.
- g. Promptly inform the VAMHCS Research Service of any allegations of noncompliance associated with VAMHCS Human Subjects Research.
- h. Appoint VAMHCS representation to each University IRBs that is an IRB of record for VAMHCS Human Subjects Research protocols.
 - 1. At least two members (and alternates when possible) representing the VAMHCS must be appointed to each University IRB panel that reviews VAMHCS research.
 - 2. VAMHCS representatives must be VAMHCS salaried for at least 5/8 FTE. At least one of the two VAMHCS representatives on each University IRB must have scientific expertise.
 - 3. VAMHCS representatives must be full voting members of the University IRBs (i.e. they will participate as other members, and will review all protocols, not just VAMHCS protocols, assigned to the University IRB on which they serve).
 - 4. A VAMHCS voting member must be present during full board review of VAMHCS Human Subjects Research.
- i. Promptly notify the VAMHCS Research Service of any changes to the University's FWA status.
- j. Maintain a current FWA. The University agrees that it will not involve the VAMHCS in any activities with a collaborator that does not have a FWA.
- k. Develop policies and procedures that detail how compliance monitoring, audits, and reporting to appropriate regulatory authorities will be handled by administrative officials, compliance officers, and the University IRBs and its administrators. Report the results of any external monitoring or audits of research activity at the University that impact upon VAMHCS Human Subjects Research or the status of the VAMHCS Human Subjects Research protection program including visits by sponsors and regulatory/compliance bodies.
- l. Actively cooperate with the VAMHCS in resolving any problems encountered in either the University or VAMHCS human research protection program, and, if this fails, terminate this MOU as provided below.
- m. Ensure that all University IRBs members and IRB Chairs have received the appropriate training as University IRBs members. Facilitate training that will ensure University IRBs members are knowledgeable about applicable VAMHCS policies if those members sit on a University IRBs that will review VAMHCS protocols.
- n. Appoint a representative of the Dean's Committee (or its equivalent) to the VAMHCS R & D Committee.
- o. Require that the VA Form 10-1086, which includes specific

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

indemnification and notification clauses, will be used as the informed consent form for all VAMHCS Human Subjects Research.

- p. Maintain VAMHCS Human Subjects Research records at University for 5 years following project termination in accordance with VAMHCS Policy. Provide the VAMHCS ready access to these records for review and/or copying. Consult with the VAMHCS, and transfer such records to the VAMHCS if requested, before destruction of any records maintained by the University IRBs.
- q. Assure that research is conducted in compliance with the HIPAA.
- r. Advise VAMHCS of requirements for reporting Conflict of Interest for IRB members.
- s. Handle potential conflicts of interest (financial and scientific) for VAMHCS investigators, staff, committee members and institutions (including the VAMHCS and BREF) according to University's policies and procedures and any applicable VA policies.

1.4. BREF, established under 38 USC §§7361-7368, facilitates VAMHCS Research and is subject to the policies and procedures contained in VA manuals, regulations and statutes. Principal Investigators and research personnel working on research funded through the BREF are engaged in VA Research and subject to all VA and University IRBs policies and procedures governing human subjects research.

1.5. Through communication with the Executive Director of the University HRPO, the VAMHCS will provide the University IRBs and the University HRPO with all relevant documents needed to enable the University IRBs to identify and describe or incorporate such VAMHCS policies and procedures into the University IRBs policies and procedures. The University IRBs policies and procedures will be available to all VAMHCS Research investigators and research personnel via the University HRPO web site.

1.6. The University IRBs policies and procedures will specify that they apply to all physicians, scientists, health care workers and other research personnel participating in VAMHCS Research except where specifically stated.

1.7. At least one University representative, nominated by the Dean of the School of Medicine ("Dean") and approved by the Director of the VAMHCS ("Director"), shall sit on the VAMHCS R&D Committee as required by VA policies. University representatives appointed to sit on the VAMHCS R&D Committee who do not otherwise have a VAMHCS appointment will be given a without compensation ("WOC") appointment by the VAMHCS provided the representative qualifies for a WOC appointment.

1.8. The VAMHCS will provide resources (direct funds and/or in-kind resources) to the University appropriate to the impact of maintaining the human research protections program involving VAMHCS Human Subjects Research. The amount and/or form of the

**VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)**

resources will be determined jointly by the University and the VAMHCS on an annual basis but will not be less than \$100,000. The amount will be determined each September for the next federal fiscal year. The University will annually invoice the VAMHCS for the agreed upon amount and payment by VAMHCS will be made within 3 months after receipt of the invoice or within 3 months after the annual Federal budget has been signed by the President of the United States.

1.9. The University, VAMHCS and BREF will collaborate to facilitate the Association for the Accreditation of Human Research Protection Programs, Inc. (“AAHRPP”) accreditation processes for both institutions and any associated AAHRPP audits or continuing reviews.

1.10. As part of the AAHRPP accreditation and quality improvement processes, the VAMHCS, at VAMHCS expense, will perform an oversight review of the University IRBs no less than annually and more frequently if necessary to ensure that the University IRBs is in compliance with this MOU. Such a review shall include an: assessment of the qualifications and experience of the University IRBs chair when a new chair is appointed; review of the University IRBs and its membership for appropriate composition given the research being reviewed; review of University IRBs minutes (on a monthly basis) for adherence to VAMHCS and federal requirements; review of the University IRBs policies and procedures to assess the adequacy of the review, approval and oversight criteria for VAMHCS Human Subjects Research; and an appraisal of the adequacy of University IRBs resources, including an appropriate number of University IRBs committees for the volume and types of research being reviewed and being conducted subject to University IRBs oversight.

1.11. The University policy on disclosures of Conflict of Interest to the University IRBs shall be applicable to VAMHCS Human Subjects Research in the same manner as it is applicable to other research subject to University IRBs review. VAMHCS employees appointed to the University IRB will be subject to the University IRBs Conflict of Interest Policy for University IRBs Members and any applicable VA policies.

Article 2. Composition and Education

2.1. The VAMHCS agrees that the current compositions of the standing University IRBs are suitable to protect the rights and welfare of the subjects of VAMHCS Human Subjects Research.

2.2. For VAMHCS representatives officially appointed to the University IRBs, their service will be within the scope of federal employment with liability claims related to such service being subject to the Federal Tort Claims Act. A VAMHCS representative who is a member of the University IRBs will not be considered State of Maryland personnel for purposes of the Maryland State Tort Claims Act unless the VAMHCS representative is also a University employee or has a University appointment. If both the

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

federal and state tort claims acts apply, the federal coverage shall be primary coverage for the VAMHCS representatives.

2.3. VAMHCS representatives on the University IRBs shall meet all initial and ongoing training requirements for University IRBs membership as outlined in the University IRB policies and procedures.

Article 3. IRB and R&D Committee Review and Oversight

3.1. The University IRBs shall perform initial and ongoing protocol review of VAMHCS Research in accordance with 45 CFR 46 (Common Rule) Parts A B, C and D, 38 CFR 16, 21 CFR 50 & 56, and VA policies, directives and handbooks relevant to reviewing and approving VAMHCS research, provided the Principal Investigator for such research has a faculty appointment at the University, and further provided that if the Principal Investigator has multiple faculty appointments, the appointment at the University is the primary faculty appointment.

3.2. The University IRBs have the authority to

- a. approve, require modifications to secure approval, and disapprove all human subjects research activities overseen and conducted by the VAMHCS;
- b. suspend or terminate approval of human subjects research subject to this MOU that is not being conducted in accordance with the University IRB's or VA's requirements or that has been associated with unexpected serious harm to participants;
- c. observe, or have a third party observe, the consent process and the conduct of the research under the auspices of the VAMHCS or BREF that is subject to this MOU.

3.3. The University IRBs will identify and include in the review of VAMHCS Human Subjects Research, members or ad hoc members of the University IRBs whose participation is necessary for the protection of vulnerable populations as described in federal regulations, such as veterans and prisoners. The VAMHCS will make reasonable efforts to provide members or ad hoc members with specialized expertise upon the request of the University.

3.4. The VAMHCS R&D Committee shall perform its own review of VAMHCS Human Subjects Research to ensure the scientific quality of the research and protection of human rights and to advise the Director on professional and administrative aspects of the VAMHCS R&D program as required by VA policies and procedures.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

- 3.5. The VAMHCS R&D Committee does not have the authority to approve research that has not been approved by the University IRBs.
- 3.6. The VAMHCS R&D Committee shall inform the University IRBs if the Committee disapproves a research project or amendment or does not grant continuing approval for any research project, amendment or renewal that has been approved by the University IRBs. The research may continue at University of Maryland Baltimore (“UMB”) but must discontinue at the VAMHCS.
- 3.7. No agent of the VAMHCS may attempt to influence the decisions of University IRBs Committee members or Chairs.

Article 4. Reporting

4.1. The University will provide the VAMHCS Research Compliance Officer (“VAMHCS Compliance Officer”) access to all information pertaining to VAMHCS protocols submitted to the University IRBs. Currently the information is maintained in computerized form in the University’s Biomedical Research and Assurance Network (BRAAN) system. This information includes, but is not limited to, the University IRBs minutes, the status of University IRBs approval of VAMHCS Human Subjects Research, current approval and expiration dates for VAMHCS Human Subjects Research protocols, University IRBs suspensions and terminations of VAMHCS Human Subjects Research protocols, and University IRBs investigations and determinations of non-compliance with the Common Rule, other applicable standards, or University IRBs directives by investigators carrying out VAMHCS Human Subjects Research.

4.2. University IRBs policies and procedures will state that reporting of serious adverse events in VAMHCS Human Subjects Research is primarily the responsibility of the Principal Investigator, who will report simultaneously to the VAMHCS R&D Office and to the University IRBs. Independent of the Principal Investigator’s responsibility to report serious adverse events, the VAMHCS Research Office and the University will report to one another any serious unexpected or other life-threatening adverse events involving VAMHCS Human Subjects Research

4.3. On at least a monthly basis, the University will provide the VAMHCS Compliance Officer copies of the University IRBs minutes relating to VAMHCS Human Subjects Research. The VAMHCS Compliance Officer will provide the University IRBs minutes to the VAMHCS Associate Chief of Staff for Research & Development (“ACOS”). University IRBs documents, including minutes, shall be maintained confidential to the extent permitted by law by the VAMHCS and will be used only by the

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

VAMHCS R&D Committee and other persons who have a need to know the information to perform official duties. The ACOS has the primary responsibility for maintaining the continued confidentiality of University IRBs documents. The University will permit the VAMHCS Compliance Officer to audit for the Common Rule compliance, and compliance with other applicable federal rules, the portion of the University IRBs documents that pertain to VAMHCS Human Subjects Research. These audits may be done on a periodic basis as part of the VAMHCS’s own monitoring program.

4.4. The University will notify the ACOS when an oversight agency or organization initiates any action regarding human research protections non-compliance or human research misconduct and of any report to the University IRBs of allegations of investigator non-compliance, research misconduct, or research participant complaints involving VAMHCS Human Subjects Research. The ACOS will notify the Dean or the Dean’s designee when an oversight agency or organization initiates any action regarding non-compliance, research misconduct or complaints involving VAMHCS Human Subjects Research, and of any report of allegations of investigator non-compliance, research misconduct, or research participant complaints involving VAMHCS Human Subjects Research.

4.5. The VAMHCS Research Office will provide the University HRPO with the details of any internal compliance audits of VAMHCS Human Subjects Research or of the VAMHCS human subjects protections, and will notify the University HRPO when any allegation, complaint, regulatory action or inspection is initiated which involves VAMHCS Human Subjects Research. The VAMHCS Research Service will report at least annually to the University HRPO the status and resolution of such complaints, actions and inspections.

4.6. The University will provide the ACOS with details of any audits conducted by the University HRPO that involve VAMHCS Human Subjects Research.

4.7. The VAMHCS Research Office & BREF will notify the Dean or the Dean’s designee of the results of any regulatory actions and/or inspections of the human subjects protections program at the VAMHCS conducted by the VA Office of Research Oversight (“ORO”) or other state or federal agencies.

Article 5. Miscellaneous

5.1. Should the University IRBs fail to fulfill their duties and responsibilities as the IRBs of record for VAMHCS and BREF, the following remedies are available to VAMHCS and BREF:

- a. Terminate this MOU and establish an IRB at the VAMHCS.

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

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Baltimore, Maryland 21201

Baltimore, Maryland 21201

David E. Johnson, Ph.D. Date
Executive Director
Baltimore Research and
Education Foundation
10 North Greene Street
Baltimore, Maryland 21201

Sanford M. Garfunkel, FACHE Date
Network Director
VA Capital Network, VISN 5
849 International Drive, Suite 275
Linthicum, Maryland 21090

ATTACHMENT 7:

Table 1. VAMHCS Process for Protocol Approval and Study Conduct

Requirement	Process / Reason
IRB Approval (BRAAN/CICERO)	
BRAAN Protocol / 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, etc. Subjected to departmental review and the IRB “Deferral Prevention Program” as part of the approval process.
Investigator Drug Brochure, Sponsors’ protocol, grant	Provides committee with greater detail on scientific merit, potential risks to subjects, pre-clinical findings, etc.
Informed Consent Document	Must have all essential elements of Informed Consent and applicable additional elements; BRAAN/CICERO automatically provides template, including VA format; investigators must use HRPO checklist “General Requirements for Informed Consent” or a similar checklist to confirm that all requirements are in place.
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 HIPAA worksheet and authorization	HIPAA form is submitted as an attachment; must be submitted unless a waiver is requested.
Amendments (to protocol, ICF, BRAAN/CICERO information)	Submit “Modification Request” to the IRB and R&D committee; forms and process are on HRPO website (IRB) and via the Research Service (R&D Committee).
R&D / Human Subject Subcommittee Approval	
Submission Checklist	Ensures that all paperwork and sign-offs

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

	are provided.
Research Methods Accountability Form	Protects patient safety by notifying the Investigational Pharmacist and the Research Compliance Officer of drugs to be used in studies, arrangements for storage & dispensing, training of staff, etc.
<ul style="list-style-type: none"> • Attestation for the Use of Devices • Attestation for the Use of Equipment in the Conduct of a research Study • Attestation for the Performance of Procedures in the Conduct of a Research Study 	Requires the PI to take responsibility for proper training of staff and storage/operation of devices/equipment; protects patient safety by notifying the Research Compliance Officer of research-related devices, equipment and procedures to be used in studies (even if they are not investigational), arrangements for storage & dispensing, training of staff, etc.
Clinical Trials Data Sheet	Gathers information on the use of VAMHCS resources, plans for reimbursement, establishment of research clinics, etc.
Training, Licensing & Credentials Database	Currently an Excell spreadsheet updated continually as certifications are submitted; VetPro/RNs
Amendments (to protocol, ICF, BRAAN/CICERO information)	Submit “Modification Request” to the IRB and R&D committee; forms and process are on HRPO website and available from Research Service.
Recruitment/Enrollment Requirements	
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	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.
ICF scanned into CPRS	Copy of signed ICF must be brought to Research Service; RS staff does quality checks then scan into CPRS or return to PI for clarification. Scanned forms can be

VAMHCS HUMAN RESEARCH PROTECTION PLAN
(HRP 01.02)

	accessed by all clinical staff to get information on study.
Study Conduct	
Adherence to protocol	Should be guided by 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&D Committee and IRB as necessary.
Adherence to DSMP	
Adherence to Research Methods Accountability Forms	
Reporting of "Unanticipated Problems Involving Risk to Subjects or Others" and other reportable events	PIs are required to report 'Unanticipated Problems' and other reportable events to the IRB and the Research Service (ORC) via BRAAN/CICERO when they occur or in continuing review (depending on IRB P&P I.3.J); routine or for-cause audits assess investigator compliance; reported to Research Compliance Officer and R&D Committee and IRB as necessary.