HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

1. **POLICY**

The Birmingham VA Medical Center (BVAMC) Human Research Protection Program (HRPP) program is committed to its mission of fostering a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the BVAMC.

It is the policy of the BVAMC to ensure the compliance with all VA policies as well as all federal, state, and local laws and regulations. As outlined in this Standard Operating Procedures (SOP), the BVAMC has a systematic and comprehensive HRPP with qualified and appropriate leadership. If at any time there is a discrepancy between local and national regulations regarding the protection of human subjects in research this facility adheres to the most stringent regulation as it applies to each individual situation. All research conducted at the BVAMC involving human participation and/or clinical investigations of FDA-regulated test articles are subject to the BVAMC HRPP policies and procedures.

This SOP establishes that BVAMC research will be carried out in an ethical manner. The Institutional Review Board (IRB) members, IRB staff and investigators are expected to follow the basic ethical principles guiding research involving human subjects in the Belmont Report. Three basic principles contained in *The Belmont Report*, are central to the ethical obligations and expectations of the IRB members, staff and investigators in research involving humans, assuring that the rights and welfare of subjects are protected. Briefly, these three principals are:

- **Respect for Persons.** Individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection (e.g. consent, privacy, and confidentiality).
- **Beneficence.** Research should always be conducted to maximize possible benefits and minimize possible risks to the persons involved.
- **Justice.** There should be equitable selection of subjects, which includes consideration of the following: purposes and setting of the research, the scientific and ethical justification for including vulnerable populations or for excluding classes of persons who might benefit from the research.

The BVAMC will abide by VHA and other Federal requirements for specific protections for human subjects. These applicable laws that govern the BVAMC HRPP include:

- The Federal Policy (Common Rule) for the protection of human subjects ([38 CFR 16] and DHHS Subpart A of the DHHS regulations at [45 CFR 46]).
• 38 CFR 17.33 (provides regulations for human subjects), 38 CFR 17.45 (addresses medical hospital care in research studies), 38 CFR 17.92 (addresses outpatient care for research studies).
• Food and Drug Administration (FDA) regulations 21 CFR 50 (informed consent regulations), 50 Subpart D (safeguards for children), 56 (IRB regulations), and 312 (investigational new drug application – IND).

On January 19, 2017, a major revision to the Federal Policy for the Protection of Human Subjects was published and subsequently revised January 22, 2018 and again June 19, 2018 that requires compliance of studies approved by the IRB or determined to be exempt by IRB on or after January 21, 2019. The revised Common Rule also allows for continued compliance with the previous 1991 Common Rule for those studies approved by the IRB or determined to be exempt prior to January 21, 2019. Additionally, studies originally subject to the pre-2018 requirements may transition to the revised Common Rule on or after January 21, 2019. If a study originally subject to the pre-2018 requirements is determined to transition to the revised Common Rule the institution or an IRB must document and date such determination. Studies that transition to the revised Common Rule must comply with the 2018 requirements on the documented date.

Between July 19, 2018 and January 20, 2019, if the research is determined to transition to the revised Common Rule the institution or IRB could decide to apply two provisions from the revised Common Rule: the revised definition of research that specifies four categories of activity deemed not research or the elimination of IRB review of the grant application or contract proposal. If any study applied either burden reducing provision, that study must be compliant with the revised Common Rule on January 21, 2019.

2. RESPONSIBILITIES

The BVAMC HRPP is an integrated program that comprises institutional officials, Research and Development (R&D) leadership, two Institutional Review Boards (IRB), investigators, monitoring bodies, and participants involved in research. HRPP functions are written in the SOP’s and distributed among the groups outlined above as well as Sponsors and the participants themselves. The overall organizational structure for protecting research participants is outlined in the BVAMC HRPP Organizational Chart, accompanying SOPs, and Medical Center Memorandums (MCM). The HRPP is responsible for establishing a formal process to monitor, evaluate, and continually improve the protection of human research participants; dedicating sufficient resources; exercising oversight of research protection; educating leadership, investigators and research staff about their ethical responsibility to protect research participants; and, providing a mechanism to intervene in research and to respond directly to concerns of research participants.

As the Institutional Official (IO) the BVAMC Director has ultimate responsibility for ensuring the structure, function, and policies of the HRPP to guarantee the protection of human subjects participating in VA-approved research. Also, the Director ensures the availability of resources sufficient to protect the rights and welfare of research participants, taking into consideration the research activities in which they are asked to participate. The Director is the signatory official for the FWA. Specifically, the Director is responsible for:
• Establishing the HRPP of the institution advised and assisted by the R&D Committee, Associate Chief of Staff of Research and Development (ACOS/R&D) and the Chief of Staff (COS).
• Establishing oversight to ensure compliance with regulations and effective administration/implementation of the HRPP.
• Implementing the R&D program, policies and procedures, including the appointment of members to the R&D Committee and any appropriate subcommittees.
• Ensuring that R&D funds are used appropriately and adequate resources, including funds and space, are provided for research and administrative functions.
• Ensuring the ethical and scientific conduct of research.
• Protection of human and animal subjects in research.
• Appointing the IRB and R&D Chairs.
• Appointing the R&D and all subcommittee members.
• Providing Research and Development Service with needed resources/staff necessary for implementation of the HRPP.
• Supporting IRB and R&D Committees, their authority and decisions.
• Establishing education and oversight mechanisms for the IRB/R&D committee members.
• Contacting Office of Research Oversight (ORO), Office of Human Research Protection (OHRP), FDA, and others as needed as the Institutional Official responsible for the HRPP.
• Setting the “tone” for institutional culture of respect for HRPP.
• Ensuring access to HRPP information and effective institution-wide communication.
• Ensuring that Investigators fulfill their responsibilities.
• Delegating authority to ACOS/R&D through the COS for the administration of Research and Development Service (VHA Handbook 1200.01, VHA Handbook 1200.05).

Chief of Staff (COS) ensures oversight of all research conducted at the BVAMC, specifically the COS is responsible for:
• Oversight of Research and Development Service.
• Oversight of the HRPP through the ACOS/R&D.
• Oversight of the R&D Committee.
• Oversight of Pharmacy including Investigational Pharmacy.
• Initiates disciplinary action with investigators as needed.
• The COS is responsible for determining (with the assistance of the IRB Chair) necessary actions to protect subjects if a study has been closed/expired/terminated or suspended.

The Associate Chief of Staff for R&D (ACOS/R&D) ensures that the HRPP is operational and properly implemented. The BVAMC Director delegates responsibility for the BVAMC HRPP to the ACOS/R&D, (through the COS) who is an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program. Specifically, ACOS/R&D is responsible for:
• Administration of the facility’s R&D program, including oversight of the operations of the R&D Committee and subcommittees.
• Implementation of the Human Research Protection Program (HRPP).
• Management of the Research Program.
• Implementation of R&D Committee decisions.
• Implementation of IRB decisions.
• Providing staffing and infrastructure for continuity and consistency of the HRPP.
• Participation with the Medical Center Director in the management of the facility’s health care programs, particularly in those areas where integration of R&D Service can have a beneficial effect on patient care.
• Financial management of R&D Service.
• Assurance that all research staff adheres to the ethical conduct of research, and for the protection of human subjects (including personal data) and animals in research.
• Monitoring changes in VA and other federal regulations and policies that relate to Research including the HRPP.
• Approving all correspondence to other agencies regarding the HRPP and assures the involvement of the appropriate officials within the institution and at VA Office of R&D, ORO and OHRP.

The IRB Chairperson is responsible for chairing IRB meetings in an orderly manner with procedures defined by Robert’s Rule of Order and following the HRPP SOPs as published.
• The IRB Chair person (or designee) is responsible for assisting investigators in determining when studies meet the regulatory definitions of human research and require IRB review.
• The IRB chair or designee determines if submitted research can be approved using expedited procedures or if the study meets federal regulations for an IRB exemption.
• Once determined the IRB chair is responsible for conducting the expedited review, and forwarding exempt research to the R&D Committee. See SOP #4 Expedited Review and #5 Exempt Research for more details.
• The IRB Chair is responsible for reviewing each protocol submitted to the IRB to evaluate and assure there is at least one IRB member who is knowledgeable or experienced with such participants who may be vulnerable to coercion or undue influence.
• The IRB Chair is responsible for notifying the COS and working with him/her to determine what is necessary to protect the subjects, when subjects are at risk due to a suspended/expired/terminated or closed study.
• The IRB Chair evaluates all adverse events reported to the IRB to determine the seriousness of the event and whether or not it meets the criteria for reporting to the BVAMC Director and ORO as outlined in VHA Handbook 1058.01 Research Compliance Reporting Requirements.

Research Compliance Officer (RCO) assists the ACOS/R&D in ensuring that the HRPP is operational and properly implemented. The RCO oversees HRPP education, quality improvement, and compliance audits. The RCO ensures that the HRPP SOPs governing research are readily available to investigators, research staff, and anyone affiliated with the BVAMC in order to ensure that these individuals are informed about their responsibilities.
when conducting research with human subjects. The RCO is responsible for disseminating new information that may affect the HRPP, including laws, regulations, policies, procedures, and emerging ethical and scientific issues. Specifically, the RCO is responsible for:

- When research is proposed under the auspices of the Department of Defense (DoD), IRB staff, chairs, members and investigators and their staff are informed of these requirements by the RCO. The RCO will communicate directly with the IRB at the respective IRB meeting. The IRB will, in turn, inform the investigator and their staff.
- Assisting Investigators and all research staff with completion of necessary training to protect human subjects as required by VHA, VA, federal and state regulations.
- Providing new Investigators and Coordinators with training and New Investigator materials.
- Providing HRPP training on a regular basis to coordinators, Investigators and others as needed to keep all informed of new and changing policies.
- Assurance that all research including human research is conducted ethically and in compliance with all BVAMC HRPP, VA, VHA, FDA, federal, and state regulations.
- Assists the A/O, ACOS of R&D to update as necessary all Standards of Operation for BVAMC Research according to all VA, VHA, federal and state regulations.
- Regular contact with VISN 7 Research Compliance Officer, IRB Chair and the IRB administrator as needed with issues of concern regarding compliance with research activities.
- Assuring that Pharmacy Service is compliant with all regulations and SOP’s regarding investigational drugs in research studies for the protection of human subjects.
- Annually evaluates the HRPP and reports results to the Institutional Official through the ACOS/R&D, and the IRB and R&D Committees.
- Assist the A/O and ACOS to prepare Research Service for any and all regulatory compliance and accreditation issues (including any necessary updates) such as VA HRPP accreditation, Federal Wide Assurance and IRB registration with OHRP.
- Auditing individual studies every three years (more often if necessary) to assure that all HRPP polices are adhered to and reports any noncompliance to the IRB, IRB Chair, and/or ACOS/R&D.
- Attending and evaluating the IRB meetings, process, and study files etc. for compliance with federal and state regulations.
- Assurance that all research staff adhere to the ethical conduct of research, protecting human subjects (including their personnel data) by conducting regulatory audits every three years of individual studies (more often if necessary) along with yearly informed consent document audits. The results of audits are reported to the IRB, IRB Chair, and/or ACOS/R&D.
- Within 5 business days of identifying apparent serious or continuing noncompliance based on an informed consent audit, regulatory audit, or other systematic audit of VA research, an RCO must report the apparent noncompliance directly (without intermediaries) to the facility and then immediately to the ACOS/R&D and IRB Chair. In the absence of these two individuals, it will be reported to the Acting ACOS/R&D and Alternate IRB Chair.
- Updating HRPP staff of any changes in VA and other federal regulations and policies that relate to human subjects and/or the protection of human subjects.
• Working with the Safety Committee members and Safety Office personnel to assure that all Research is in compliance with VA, VHA, federal and state regulations.
• Prepares correspondence from Research Service to ORO, OHRP, and FDA if necessary, General Counsel of the VA and any other federal or state agency for the IO thru the ACOS/R&D. Correspondence is reviewed by ACOS/R&D prior to sending it to the IO for submission to the respective agencies.

The IRB Administrator is responsible for the following:
• Preparation of study submission packets for IRB members to review prior to IRB meetings.
• Distributing packets to IRB members.
• Preparing agenda for IRB meetings.
• Maintaining/ tracking all IRB members’ training, CV’s or resumes and appointment letters.
• Maintaining/ tracking all HRPP personnel training certificates.
• Maintaining up to date knowledge of federal regulations regarding research involving human subjects.
• Submitting study submission packets as is applicable to the Radiation Safety Officer and Pharmacy for review and approval.
• Working closely with the RCO for Research at BVAMC.
• As appropriate completes any necessary follow-up actions concerning the HRPP.
• Maintaining the IRB database.
• Preparing correspondence from IRB to Investigators, Coordinators, ACOS/R&D and the Medical Center Director as appropriate.
• Informing the following individuals (either by phone, email or in person) of any noncompliance or regulatory issues that may arise with Investigators who have a research project: IRB Chair, ACOS/R&D, AO/R&D and the Research Compliance Officer. The ACOS/R&D and/or IRB Chair will determine (with input from all above) if reports are required to the BVAMC Director and/or other outside agencies. If the IRB Chair and/or ACOS/R&D are unavailable for determining who should be contacted then the AO/R&D and/or the RCO will make that determination.
• Informing the RCO of all reported changes to studies including but not limited to; changes in staff, protocol deviations, protocol violations, SAE’s, AE’s, lack of training documentation and any other item that may cause harm to subjects, and/or that is viewed as noncompliance.
• Informing the RCO of new Investigators to assure they receive training and materials designed for new Investigators.
• Preparing the IRB minutes.

BVAMC Research and Development (R&D) Committee is responsible to the IO for maintaining high standards throughout the facility’s R&D program assuring compliance with applicable federal, FDA, VA, state and local regulations. These standards include assuring the scientific and ethical quality of research studies, protection of human subjects in research (including protecting personal data), laboratory safety, and the welfare of animals in research. The Committee advises the IO on professional and administrative aspects of the R&D Program. All R&D activities within the facility, whether funded or unfunded, are within its
purview. Scientific review of research studies is a prime responsibility of the committee. The BVAMC IRB and the VA Central IRB (CIRB) are subcommittees of the R&D Committee. The R&D Committee is responsible for ensuring the Information System Security Officer (ISSO) and Privacy Officer (PO) review is complete before a study is given final approval. The R&D Committee is responsible for establishing a local R&D Conflict of Interest Committee. Full responsibilities and procedures of the R&D Committee are detailed in MCM 151-01 and R&D Committee SOP’s.

The Research and Development Coordinator is responsible for the following:
- Preparation of submission packets of Exempt studies for R&D Committee members to review prior to R&D Committee meetings.
- Distributing packets to R&D Committee members.
- Preparing the agenda for R&D meetings.
- Preparing correspondence from ACOS/R&D to Investigators, as appropriate.
- Preparing the R&D Committee minutes.

Both the BVAMC IRB and the CIRB have the responsibility and authority to approve, require modifications (in order to secure approval), disapprove research activities, or suspend research activities (covered by VHA Handbook, 1200.05), regardless of whether the research is funded or non-funded. The full responsibilities and procedures of each IRB (and each IRB Chair) are detailed in, the BVAMC HRPP SOP’s #2 - 23 and MCM 151-03 and the CIRB Standard Operating Procedures.

Investigators (Principal and Co-investigators) are responsible for conducting their research in accordance with all agreements with the IRB. Investigator responsibilities are detailed in BVAMC SOP #13. All investigators are required to comply with all relevant research-related policies and procedures. All requests to conduct research involving human subjects must be submitted in accordance with the requirements set forth in the BVAMC HRPP SOPs.

The BVAMC Privacy Officer is the authoritative source for privacy within VHA and is responsible for developing and implementing a VHA Privacy Program; developing, issuing, reviewing and coordinating privacy policy for VHA in conjunction with policy efforts by VA; coordinating requirements and monitoring compliance with all Federal privacy law, regulations and guidance within VHA; and issuing direction on VHA privacy policies, practices and activities to the field. Specifically, the BVAMC Privacy Officer is responsible for ensuring the facility’s overall compliance with privacy policies and requirements, ensuring the facility has a process to review all IRB-approved VA research for compliance with privacy requirements, reporting incidents regarding protected health information (PHI) to the Privacy Violation Tracking System and participating in the investigation of such incidents, and ensuring all employees are trained on privacy annually.

3. DEFINITIONS

See HRPP SOP #24 HRPP DEFINITIONS

4. PROCEDURES
The BVAMC has a current approved Federal Wide Assurance (FWA #00001239). The BVAMC and the BVAMC IRB are committed to fulfilling and implementing the FWA commitments, regardless of sponsorship or regulatory oversight. The Director of the BVAMC is the official responsible for the FWA. Copies of this assurance are available to all investigators, IRB members, R&D Committee members, and Research Staff upon request.

The BVAMC HRPP has and follows written policies and procedures governing research with research participants that are available to investigators, IRB and R&D Committee members and research staff affiliated with the BVAMC. Such procedures are coordinated with each IRB (BVAMC IRB and the CIRB) and the Research and Development (R&D) Committee. As outlined in the IRB SOP, the BVAMC has and follows written policies and procedures that allow the IRB to function independently of other organizational entities in its role in protecting research participants. Research subject to the BVAMC HRPP does not commence until the research has received all approvals required by the BVAMC, which includes IRB approval (if human subjects research) and R&D acknowledgement with a final acknowledgement letter from the ACOS/R&D. Transnational or International Research that falls under the definition of International Research must follow the guidelines in the originating country (if lead site) or the guidelines of this country if the United States is the lead site. Please see HRPP SOP #3 Initial Review for review requirements for research conducted at multiple sites. The IRB SOP’s and R&D MCM describe the communication and interaction between these two committees, as well as entities within the organization that are involved in the conduct of human research (i.e. laboratory, pharmacy, radiology, and clinical services).

The BVAMC HRPP has and follows written policies and procedures for the following functions:

- To maintain an independent IRB (SOP#2; MCM 151-03)
- To review the proposed research study in regard to design, safety, protection of human research participants, and all other requirements prior to the initiation of the research (SOP#3) and at follow-up intervals not to exceed one year (SOP#6).
- To review the scientific or scholarly validity of a proposed research study (MCM 151-01).
- To define and provide a mechanism for expedited review of items or research that meet the requirements for expedited review (SOP#4).
- To determine when studies are exempt from applicable federal, state, and local BVAMC policies and procedures and addressing protection of participants in research exempt from applicable federal regulations (SOP#5).
- To define requirements for informed consent, to determine when studies are allowed to waiver or altered informed consent (SOP#7).
- To address patient recruitment, selection practices, and vulnerable subjects (SOP#8).
- To identify, manage, and minimize individual conflicts of interest of investigators and to recognize and manage institutional conflicts of interest (SOP#9A, SOP#9B).
- To address research privacy and data security requirements (SOP #10).
- To address reporting requirements for adverse events, protocol deviations, modifications, and unanticipated problems involving risks to research participants or others (SOP#11).
• To contribute to the improvement of qualifications/expertise and ensure compliance with continuing education requirements for all investigators, IRB and R&D reviewers and committee members, and research staff. All personnel reviewing, conducting, or supporting human research demonstrate and maintain sufficient knowledge of the ethical principles and federal, state, and local requirements for protecting research participants (SOP#12).

• To address investigators’ responsibilities and means to allow investigators to bring forward concerns or suggestions regarding the HRPP, including the IRB review process (SOP #13).

• To address participant outreach (SOP#14)

• To address DNA research (SOP #15)

• To work with sponsors, investigators, research participants, and the IRB to uphold ethical standards and practices in research (SOP#16).

• To monitor, measure and improve HRPP effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws (SOP #17 and #17B)

• To address allegations and findings of non-compliance with HRPP requirements (SOP#18).

• To address HRPP number of IRBs, budget, resources, and annual reporting requirements (SOP#19)

• To address HRPP changes with a modification/amendment review process (SOP #20)

• To address the use of any investigational or unlicensed test article in compliance with all federal, state, or local regulations (SOP #22)

• To address and ensure that the handling of investigational or unlicensed test articles meets organizational standards relating to pharmacy, inventory control, and documentation (Procedure for Investigational Drugs SOP #21 & MCM 119-20 Medication Management Policy).

• To address emergency use of a test article/humanitarian use device (HUD) (SOP #23)

The types of research typically covered by the BVAMC HRPP are clinical investigations of the cause, evaluation, assessment, treatment, or outcome of clinical medical and psychiatric illnesses. The categories of participants typically covered by the BVAMC HRPP are adults (any age over 19 years), any race or ethnicity, any gender, and nonprisoners. The BVAMC does not conduct research with children, prisoners, pregnant women (as the focus of the study), fetuses, or neonates.

The BVAMC HRPP may consult with VA Regional Counsel for guidance about regulatory compliance on issues, such as those regarding:

• Areas in which federal and state law differ relevant to human subject research

• Application of laws other than federal law relevant to human subject research

• Application of laws beyond federal law relevant to human subject research

• Contracts or legal agreements

• Travel request to ensure ethical compliance
• Questions concerning legally authorized representative when an adult is unable to provide consent, when needed, and not otherwise addressed in SOP #7 Research Informed Consent

5. REFERENCES
• 21 CFR 50, 56, 312
• 38 CFR 16.102 (b),(g) and 16.103(a), (b)(1) and (c)
• 38 CFR 17.33, 17.45, 17.92
• 45 CFR 46.103(a), (b)(1) and(c)
• VHA Directive, 1200.05 Requirements for the Protection of Human Subjects in Research

6. ATTACHMENTS
• BVAMC R&D Medical Center Memorandum, 151-01
• BVAMC R&D Medical Center Memorandum, 151-03
• BVAMC HRPP Organizational Chart
• BVAMC Federal Wide Assurance (FWA #00001239)

7. RESCISSIONS

Human Research Protection Program SOP #1 January 1, 2011; August 1, 2011; January 14, 2013, June 19, 2013, reviewed January 1, 2016, January 1, 2019

8. REVIEW DATE

January 1, 2022

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