Conduct of Research under the Oversight of the National Cancer Institute Central IRB (NCI CIRB)

1. **PURPOSE:** To describe the standard operating procedures (SOPs) for the use of the National Cancer Institute Central IRB (NCI CIRB) for cancer studies performed at Minneapolis VA Health Care System (MVAHCS). This HRPP SOP is supplemental to the MVAHCS HRPP/Research Service SOPs located on the MVAHCS Research SharePoint Site and the NCI CIRB SOPs located at https://ncicirb.org/about-cirb/sops.

2. **POLICY:** Oncology studies performed at the MVAHCS may rely on the services of the NCI CIRB for review of certain human studies. Under its Federal-wide Assurance (FWA00001480), MVAHCS is considered to be the Signatory Institution. Although not the IRB of record for these studies, the MVAHCS IRB will function in an advisory capacity to the Research & Development Committee (RDC). Oncology studies under the purview of the NCI CIRB at MVAHCS may not enroll nonveterans, prisoners or children.

3. **RESPONSIBILITIES:**

Institutional Official Responsibilities

- Appoints in writing the Signatory Institution Primary Contact (SIPC)
- Reports serious unanticipated problems and serious and/or continuing noncompliance originating at MVAHCS as required by VA policy to the Office of Research Oversight (ORO) and external federal agencies or oversight bodies.
- Updates and signs the FWA and VA Addendum.
- Signs the Institutional Agreement/Division of Responsibilities Agreement with the NCI CIRB. A copy of the signed agreement is provided to the Office of Research Oversight (ORO) each time it is updated.

Signatory Institution Primary Contact (SIPC) Responsibilities

- The ACOS/R in consultation with the IRB administrator and the RDC Chair will designate a research service employee to serve as SIPC.
- Submits initial applications to the NCI-CIRB, after reviewing the application and obtaining ACOS/R approval on behalf of the RDC.
- Receives correspondence on project approvals, renewals, and determinations from NCI CIRB and processes them according to local SOPs.
- Receives Continuing Review approval from the NCI CIRB and notifies the study team that they may use the renewed study documents that come from CIRB (informed consent and HIPAA Authorization).
- Receives a copy, per NCI CIRB SOPs, of any NCI CIRB determinations that must be reported by the NCI CIRB to federal regulatory agencies. (Note: The MVAHCS IO is still required to report to ORO and other federal bodies on behalf of MVAHCS. NCI does not report for VA).

- Promptly notifies the RDC and Research Compliance Officer (RCO) of any potentially reportable determinations received from NCI CIRB involving MVAHCS per VHA Handbook 1058.01. The ACOS/R and Institutional Official (IO) will be notified of any significant and/or reportable determinations. Assures all local processes (e.g., SRS review) are completed following NCI CIRB approval and prior to ACOS/R's authorization to initiate research.
- Notifies the RDC in advance of a plan to replace the PI so RDC can consider the qualifications of the candidate and give a written approval prior to submitting the change to NCI CIRB. Works with the local study team to maintain study team changes in the Research protocol tracking system.
- Ensures training is current for all members of the study teams prior to their inclusion in the NCI CIRB application. Works with the local study teams to ensure training is completed/current for new members of the study teams.
- Tracks NCI cancer studies through the Research protocol tracking system.

Research & Development Committee Responsibilities

- Ensures that NCI CIRB requirements for enrollment of the Institution and submission of local context forms are met. Completes and submits the Annual Signatory Institution Worksheet About Local Context, and any other worksheets/forms required by the NCI CIRB for participation.
- Oversees the conduct of the research and monitors protocol compliance.
- Reviews initial and ongoing qualifications of Investigators and research staff.
- Provides a mechanism to receive and address concerns from local study subjects and others about the conduct of the research.
- Investigates, manages, and provides notification to the NCI CIRB of any study-specific incidents, experience, or outcome that may rise to the level of an unanticipated problem and/or serious or continuing noncompliance. When notifying the NCI CIRB of a potential unanticipated problem and/or serious or continuing noncompliance, the MVAHCS RDC must provide a plan to manage the incident, experience, or outcome, including measures to prevent similar occurrences.
- Conducts annual review of NCI CIRB.
- Reviews the proposed application, and determines whether a study under purview of NCI CIRB should be conducted at MVAHCS.
- Reviews the Study-Specific Worksheet About Local Context to open a study.
- Ensures that prisoners, non-veterans and children are excluded from enrollment.
- If the NCI CIRB makes a determination involving MVAHCS, ensures the necessary input from relevant individuals is obtained when considering local MVAHCS responsibilities.
- If the study involves pregnant women, ensures facility Director approval for inclusion of this vulnerable population per the requirements of VHA Directive 1200.05 and ORD guidance.

MVAHCS IRB Responsibilities

- Serves in an advisory capacity to the RDC for research overseen by the NCI CIRB.
- Reviews requests for HIPAA Waiver of Authorization for subject recruitment activities. A qualified IRB member will be designated by the IRB chair or the IRB administrator to perform the review. These reviews will then be documented in the IRB minutes and forwarded to the RDC prior to final review and approval decision by the RDC.

- In the event of the incarceration of a MVAHCS study subject enrolled in a study overseen by the NCI CIRB, the MVAHCS IRB will determine at a convened meeting whether the subject should continue in the study. This determination will be sent to the RDC for a final decision.

Investigator Responsibilities

- Completes Annual Investigator Worksheet About Local Context.
- Initiates MVAHCS study documents per MVAHCS Policy.
- Incorporates NCI CIRB-approved boilerplate language into the NCI CIRB-approved model consent form to create the consent form to use for a specific study:
  a) Makes no language changes to the consent form with the exception of NCI CIRB-approved boilerplate language and approved VA specific language. If this results in contradictory language in the informed consent document, the investigator and/or the study team member obtaining consent will point out and explain the discrepancy to the subject.
  b) Obtains NCI CIRB approval of study-specific changes to the boilerplate language prior to implementation; and
  c) Obtains NCI CIRB approval of translations of the consent form prior to implementation.

- Develops a recruitment plan. If potential subjects are to be identified from CPRS, requests and obtains a waiver of HIPAA authorization from the MVAHCS IRB to view records as necessary.
- Maintains a regulatory file for each study under NCI CIRB purview.
- Provides updates in a timely manner to the SIPC and MVAHCS Research Office staff whenever a MVAHCS Principal Investigator is replaced, or study personnel are added or removed.
- Maintains compliance with state, local, or institutional requirements related to the protection of human subjects.
- Notifies the SIPC if a subject becomes incarcerated during participation in a study.
- Evaluates the levels of decision making capacity for subjects prior to and throughout their study participation to ensure that their informed consent is still valid. The Investigator, if not the treating physician, will confer with the treating physician to decide whether continuation in the study is in the best interest of the individual. The Investigator will seek other advice as needed.
- Forwards necessary Continuing Review materials to the MVAHCS IRB Coordinator once uploaded by NCI CIRB. Should the study not receive renewal by the end of the approval period then the study approval is expired and Investigator must stop all research activity. (Procedures for notification of the Associate Chief of Staff/

Research [ACOS/R] and the RDC are found in the MVAHCS Human Research Protection Program SOP.)

- Reports to the NCI CIRB all unanticipated problems involving risks to subjects or others, local unanticipated serious adverse events, apparent serious or continuing noncompliance, termination or suspension of research, complaints from subjects or others; and privacy or information security incidents related to VA research, including (a) inappropriate access, loss, or theft of PHI; (b) noncompliant storage, transmission, removal, or destruction of PHI; or (c) theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with VHA Handbook 1058.01 and MVAHCS Res SVC-RD-005 Reporting Research Events SOP.
- Ensures that a management/remediation plan is developed, with advice from the ACOS/R and the HSS if necessary, for local unanticipated problems and serious or continuing noncompliance.

Research Compliance Officer Responsibilities

- Conducts audits to ensure compliance with applicable federal, VA, and local policy.
- Submits audit reports with no findings to the RDC in accordance with the RCO Auditing Plan.
- Reports any study-specific incident, experience, or outcome that may rise to the level of an apparent unanticipated problem and/or apparent serious or continuing noncompliance per the requirements of VHA Handbook 1058.01 to the study team and the R&D Committee (RDC).
- *Note: According to the Authorizing Agreement, the NCI CIRB does not oversee the conduct of the study. Therefore, the audit reports with no findings do not need to be sent to the NCI CIRB. Only audit findings with an apparent unanticipated problem and/or apparent serious or continuing noncompliance should be submitted to NCI CIRB. The RCO must assure that the PI uploads audit reports identifying apparent serious or continuing noncompliance to the NCI CIRB within 5 business days of discovery.* Ensures that the NCI CIRB is notified when a regulatory deficiency has been cited on an audit that occurred during the time that the NCI CIRB was responsible for study review.
- Reports local deaths, serious adverse events, serious problems, and apparent serious or continuing noncompliance to the Office of Research Oversight (ORO) per VHA Handbook 1058.01and MVAHCS Res SVC-RD-005 Reporting Research Events SOP.

4. PROCEDURES:

Prior to initiating any studies, the PI must submit the Annual Investigator Worksheet About Local Context to the SIPC. Following review by a representative of the RDC, the worksheet can then be submitted to the NCI CIRB. Once the worksheet is approved by the NCI CIRB, the PI is eligible to submit for specific NCI CIRB-reviewed studies.

To Initiate a New Study

(1) Investigator submits the Study-Specific Worksheet About Local Context to the NCI CIRB using CTEP site number: MN015.

(2) Investigator determines if the study team has access to the NCI CIRB Participant Area. If not, Investigator contacts SIPC to provide access to NCI CIRB Participant Area. If yes, contacts SIPC to request package for NCI modified initial submission.
(3) Investigator submits required documents to the NCI CIRB for review.
(4) Investigator receives the NCI CIRB approval letter and the approved informed consent document.
(5) After NCI CIRB approval is obtained, Investigator submits an abbreviated application in the MVAHCS Research electronic protocol management system. In addition to the questions in the abbreviated application, the following documents will be submitted:
   a. HIPAA Authorization form
   b. NCI CIRB-approved informed consent document
   c. Protocol
   d. Research Financial Conflict of Interest Statements for each Investigator on the MVAHCS study team
(6) The Investigator receives a memo documenting approval of the Waiver of HIPAA authorization document and documentation of PO and ISO approval from the MVAHCS IRB.
(7) The Investigator receives documentation of the review/approval by the Subcommittee on Research Safety (SRS).
(8) The submission will be noted in the Research protocol tracking system with the NCI CIRB as the IRB of record.
(9) The SIPC will forward the approvals of the NCI CIRB, the MVAHCS IRB, and the SRS to the RDC.
(10) Following approval by the RDC, the Associate Chief of Staff/Research (ACOS/R) will issue a document authorizing the initiation of the research and then the PI may initiate the study.

Study Procedures/ Amendments/ Continuing Review

(1) For studies under a Certificate of Confidentiality, an EHR progress note entry should indicate only that an individual has been enrolled in a research study, any details that would affect the subject's clinical care, and the name and contact information for the Investigator conducting the study. Subjects' informed consent and HIPAA authorization documents are not to be included in the health record and should be kept with the study files.
(2) Study team submits proposed staff changes to the SIPC to verify required training is documented. Upon verification, the Investigator/study staff adds, changes, or removes personnel by submitting an updated contact form (see https://ncicirb.org; "How to Join" menu, click "Update Personnel or Institution Information" and use the Personnel Signatory Institution form found under the "Personnel Updates" subheading).
   a. The addition of personnel must be requested in the MVAHCS Research electronic protocol management system. If adding an Investigator, a Research Financial Conflict of Interest Statement must be included in the submission.
(3) Human subject protocols that require a modification/amendment must be submitted as outlined by the NCI CIRB SOP in section 8.3. After NCI CIRB approval, the amendment/modification will be communicated to the SIPC.

(4) Any revisions affecting the following require submission of a modification/amendment via the MVAHCS electronic protocol management system:
   a. Data use/storage in VA
   b. Who has access to data inside and/or outside VHA
   c. Data sources (e.g., audio, video, paper surveys, web-based surveys)
   d. Process of transmitting/sending/sharing data inside and/or outside MVAHCS (e.g., a new URL)
   e. HIPAA Authorization form
   f. Waiver of HIPAA Authorization
   g. Research Financial Conflict of Interest Statement changes for existing study personnel

(5) Upon receiving NCI CIRB Continuing Review approvals, Investigator will forward them to the SIPC. The SIPC will process them to obtain a notification from the ACOS/R to the Investigator that all continuing review subcommittee approvals are complete.

Reporting

1. Reporting will be in compliance with VHA Handbook 1058.01
2. *Serious Adverse Events* (meeting the criteria of a physical or psychological event that results in: Death or life-threatening experience, or Hospital admission or prolongation of hospitalization, or Persistent or significant disability or incapacity, or Intervention to prevent such an outcome) which the MVAHCS Investigator determines are **Unexpected**, and there is a reasonable possibility the event is **Related** to the research, are to be reported to the NCI CIRB within 5 business days.
3. *Local Unanticipated Problems* (a project-related event that is likely to substantially adversely affect the safety, rights, or welfare of human research subjects, or compliance with the protocol, VA policy, or federal regulations, or Information security or integrity of the research data) which the MVAHCS Investigator determines are **Unexpected**, and there is a reasonable possibility the event is **Related** to the research, and subjects or others are at **Greater risk of harm** than was previously known due to the incident, must be reported by the MVAHCS Investigator to the NCI CIRB Operations Office within 5 business days of becoming aware.
4. *Privacy breaches or information security events* must be reported to the MVAHCS Privacy Officer within 1 hour.
5. Local apparent serious or continuing noncompliance must be reported promptly to the NCI CIRB. This may include complaints from subjects or others, protocol deviations (as defined in the NCI "SOP for Reporting Research Events and Problems") and audit findings.
6. Suspension or termination by the MVAHCS Signatory Official will be reported to the NCI CIRB promptly.

Study Closure

Studies will be closed with the NCI CIRB using the procedures outlined in the NCI CIRB SOP 5.8.13. In addition, the study will be closed at MVAHCS by the study staff/PI notifying the RDC according to the MVAHCS study closeout procedures.

References:
NCI CIRB SOP
MVAHCS HRPP SOPs
MVAHCS Reporting SOP
MVAHCS R&D Committee SOP
VHA Handbook 1058.01
VHA Handbook 1200.05