

**Addendum to Durham VA Health Care System (DVAHCS) Human Research Protections Program (HRPP) Standard Operating Procedures (SOP) and Research and Development Committee (R&DC) SOP**

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

A Memorandum of Understanding (MOU) is in place between the Department of Veterans Affairs (DVA) Veterans Health Administration (VHA) Office of Research and Development (ORD), Office of Research Oversight (ORO) and National Cancer Institute (NCI), Cancer Therapy Evaluation Program (CTEP), Central Institutional Review Board Initiative (CIRB) for human research Involving NCI-sponsored cancer research conducted by VA Medical Facilities.

1. **PURPOSE:** To describe the standard operating procedures (SOPs) for the use of the National Cancer Institute Central Institutional Review Board (NCI CIRB) for cancer studies performed at the Durham Veterans Affairs Medical Center (DVAMC). This IRB SOP is supplemental to the Human Subjects Research Protection Program (HRPP) SOPs described in the Durham VA Research SOPs, and to the NCI CIRB SOPs.
2. **POLICY:** Oncology studies performed at the DVAHCS may rely on the services of the NCI CIRB for review of human studies. Under FWA00001600, the DVAHCS is considered to be the Signatory Institution. The DVAMC IRB will review requests for waiver of HIPAA authorizations and address VA requirements outlined below that are not managed by the NCI CIRB SOPs. The Durham VA Privacy Officer will provide review of HIPAA authorizations. Investigators must follow the NCI CIRB guidelines and must obtain Research and Development (R&D) Committee approval to engage in the conduct of these studies. Oncology studies under the purview of the NCI CIRB at the DVAHCS may not enroll prisoners or pediatric research subjects.
3. **RESPONSIBILITIES:**

**Institutional Official**

- 1) Signs the Signatory Institution Agreement/Division of Responsibilities, which takes the place of the VHA Memorandum of Understanding for use of an IRB operated by another institution. A copy must be sent to ORO each time the Agreement is updated.
- 2) Reports unanticipated problems and serious and/or continuing noncompliance originating at DVAHCS as required by VA policy to ORO and external federal agencies or oversight bodies.
- 3) Updates and signs the FWA.

**Research Office and Signatory Institution Primary Contact**

- 1) Completes and submits the Annual Signatory Institution Worksheet about Local Context, and any other worksheets/forms required by the NCI CIRB for participation. Resolves concerns related to boilerplate informed consent language.
- 2) Receives correspondence on project approvals, renewals, and determinations from the NCI CIRB and processes them according to local SOPs.
  - a. Per NCI CIRB SOPs Section 10.2.2.1, any NCI CIRB determinations (local or remote) that must be reported by the IRB to federal regulatory agencies will be reported from NCI

CIRB with copy to the DVAMC. Upon receipt of determinations involving DVAHCS, the R&D Office will promptly notify the Research Compliance Officers (RCOs) and Institutional Official. NOTE: The VA institutional Official remains legally responsible for reporting on behalf of DVAHCS, i.e., reports completed by the NCI IRB are not on DVAMC's behalf.

- 3) Tracks NCI cancer studies for the DVAHCS R&DC.
- 4) Reviews the Study-Specific Worksheet About Local Context to open a study.
- 5) Receives and addresses concerns from local study participants and others about the conduct of research per local policy outlined in DVAHCS HRPP SOP RR 403, Section 1.8.

### **R&D Committee**

- 1) During a convened meeting, the R&DC Committee will (with advice from local IRB) vote to approve, approve with contingencies, or not approve the research to be conducted at the facility.
- 2) Reviews and determines whether studies under the oversight of the NCI CIRB should be conducted at DVAHCS.
- 3) Provides final approval for VA research.
- 4) **Designated Review.** The following R&DC activities may be approved by the R&DC outside convened meeting:
  - a. Minor changes to a study, following full board review. *NOTE: R&DC may only recommend changes to local activities and documents not under the purview of the NCI CIRB.*
  - b. Final approval for studies approved contingent on the full approval of a subcommittee (e.g., Radiation Safety Committee; Subcommittee on Research Safety). *NOTE: Full approval by the subcommittee must be granted prior to R&DC approval by designated review (review outside convened meeting).*
  - c. Final approval for protocols approved contingent upon completion of PO and ISSO review.
  - d. Minimal Risk studies approved by expedited review by the NCI CIRB.
- 5) R&DC will determine, and specifically document its determination, that the research:
  - a. Supports the VA mission and is relevant to the care of Veterans.
  - b. Is scientifically meritorious.
  - c. Ensures the security of VA data, and storage of the data and specimens in accordance with all applicable requirements.
- 6) The R&DC is not required to review and approve continuing reviews and amendments that have been reviewed and approved by the NCI CIRB. The R&DC will be provided sufficient documentation in the NCI CIRB redacted or unredacted minutes that are provided to R&DC.
- 7) Oversees the local conduct of the research and monitors protocol compliance.
- 8) Ensures compliance with state, local, or institutional requirements related to the projection of human subjects research.
- 9) Conducts annual review of NCI CIRB as part of Annual Quality Assurance Review of the HRPP to ensure the obligations as detailed in the MOU and Authorization Agreement are met.
- 10) 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 institution will provide a plan to manage the incident, experience, or outcome, including measures to prevent similar occurrences.

- 11) Reviews NCI CIRB determinations of serious and/or continuing noncompliance; decides on remedial action plan required by NCI CIRB.
- 12) Has the authority to disapprove research that has been approved by NCI CIRB or by an appropriate subcommittee.
- 13) Has the authority to suspend or terminate approval of research that is not being done in accordance to HRPP policies, is not in compliance with federal regulations, or has been associated with unexpected harm to subjects.
- 14) Ensures Information System Security Officer (ISSO) and Privacy Officer (PO) review is complete prior to study approval.
- 15) Ensures review and approval by other relevant committees has occurred prior to approval, including review by the Radiation Safety Committee and Subcommittee on Research Safety.
- 16) Ensures the local Conflict of Interest Committee has reviewed all OGE Form 450-Alternative--VA, Research Financial Conflict of Interest Statement, signed by investigators.
- 17) Ensures that no prisoners are enrolled in NCI Studies.
- 18) Determines if non-Veterans should be enrolled in a NCI study per local and VHA ORD policy guidelines.
- 19) Ensures adequate resources to perform the research including proper facilities and equipment to conduct the research.
- 20) Ensures the initial and ongoing qualifications of investigators and staff.

**Facility Privacy Officer and Information Security Officer:**

- 1) The facility Privacy Officer is responsible for reviewing the HIPAA authorization for all applicable NCI CIRB protocols to ensure legal authority exists prior to the use, access, collection, creation, and disclosure of PHI by DVAHCS investigators.
- 2) Ensures disclosures and data transmission meet privacy and security requirements per VA Directive 6500, Managing Information Security Risk: VA Information Security Program, dated September 20, 2012; VA Handbook 6500, Risk Management Framework for VA Information Systems – Tier 3: VA Information Security Program, dated March 10, 2015; and VHA Directive 1605.01, any superseding policies
- 3) Identifying deficiencies in the provisions for privacy and confidentiality or information security, respectively, of the proposed research, and making recommendations to the investigator and of options available to correct the deficiencies.
- 4) Following up with the investigator, in a timely manner, to ensure the proposed research is in compliance with relevant privacy and confidentiality and information security requirements, respectively, before the investigator initiates the study.

**Durham VAHCS IRB**

- 1) While the NCI CIRB will serve as the IRB of Record for NCI CIRB studies, study teams will need to apply to both the NCI CIRB and the Durham VA IRB for approval. The review by the Durham VA IRB, through convened or expedited review procedures outlined in the HRPP SOP, is to ensure compliance with institutional requirements that are not assessed by the NCI CIRB's Local Context Committee.
- 2) Reviews and approves requests for waiver of HIPAA authorization.
- 3) Recommends to the R&DC whether the NCI CIRB study should be conducted at the DVAHCS.
- 4) Reviews any privacy or information security incidents related to VA research, including (a) any inappropriate access, loss, or theft of Protected Health Information (PHI); (b) noncompliant

storage, transmission, removal, or destruction of PHI; or (c) theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with RCO SOP, IRB SOPs and VHA Handbook 1058.01.

- 5) Reviews copies of reports submitted to NCI CIRB of unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated related serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research, complaints from subjects or others.
- 6) The local IRB cannot request changes to the approved NCI study documents.

### **Principal Investigator (PI)**

- 1) Completes Annual Investigator Worksheet About Local Context and notifies the Signatory Site Primary Contact prior to submitting to the NCI CIRB.
- 2) Completes the Study-Specific Worksheet About Local Context and notifies the Signatory Site Primary Contact prior to submitting to the NCI CIRB.
- 3) Submits initial study review request to both the DVAHCS IRB and NCI CIRB
  - a. The PI may start the local IRB submission process (e.g., submitting documents to the Information System Security Officer (ISSO) and Privacy Officer (PO) for review) prior to submission to the NCI CIRB in order to facilitate ancillary committee reviews.
- 4) Incorporates NCI CIRB-approved boilerplate language into the NCI CIRB approved DVAHCS letterhead.
  - a. Makes no language changes to the consent form with the exception of NCI CIRB-approved boilerplate language and approved letterhead;
  - 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.
- 5) Submits to R&DC OGE Form 450-Alternative--VA, Research Financial Conflict of Interest Statement, signed by investigators.
- 6) Develops a recruitment plan. If potential subjects are to be identified from the Computerized Patient Record System (CPRS), request for waiver of HIPAA authorization to view records as necessary. Waiver of HIPAA authorization must be reviewed by the PO and must be reviewed and approved by the DVAHCS IRB.
- 7) Maintains a regulatory file for each study under NCI CIRB purview.
- 8) Notifies the Signatory Institution Primary Contact immediately whenever a Signatory Institution Principal Investigator is replaced, or study personnel are added or removed.
- 9) Provides notification to the R&DC and Research Office when a Principal Investigator or study personnel is replaced, added, or removed.
- 10) Submission and approval of the Annual Principal Investigator Worksheet About Local Context prior to finalizing the replacement Principal Investigator.
- 11) Maintains compliance with state, local, or institutional requirements related to the protection of human subjects.
- 12) Notifies the DVAHCS IRB if a subject becomes incarcerated during their participation in a study.
- 13) Notifies the DVAHCS IRB if a female subject becomes pregnant during their participation in a study.

- 14) Evaluates the levels of decision-making capacity for subjects throughout their study participation to ensure that the informed consent is still valid. If individuals with impaired decision making are to be enrolled, the local policy outlined in the HRPP SOP will be followed.
- 15) Reports to NCI CIRB any unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated related serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research, complaints from subjects or others. A copy of the report will be submitted to the Durham VA IRB.
- 16) The PI is responsible for proposing/preparing a management/remediation plan for IRB review prior to submitting to the NCI CIRB for local potential unanticipated problems and possible serious or continuing noncompliance.
- 17) Reports to Durham VA IRB any privacy or information security incidents related to VA research, including (a) any inappropriate access, loss, or theft of Protected Health Information (PHI); (b) noncompliant storage, transmission, removal, or destruction of PHI; or (c) theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with RCO SOP, IRB SOPs and VHA Handbook 1058.01.
- 18) Provide notification to the Durham R&DC when a study has been closed, terminated, or suspended by NCI CIRB.

#### **Research Compliance Officer**

- 1) Conducts audits to ensure compliance with applicable federal, VA, and local policy.
- 2) 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 Durham VA IRB. The report to the NCI CIRB is sent by the Signatory Institution PI per NCI CIRB SOPs.
- 3) Submits audit reports to the local IRB. Note: According to the Authorizing Agreement, the NCI CIRB does not oversee the conduct of the study. Therefore, the audit reports do not need to be sent to the NCI R&DC. Only an apparent unanticipated problem and/or apparent serious or continuing noncompliance should be submitted to NCI CIRB by the PI.
- 4) Reports any local deaths, local serious adverse events, serious problems, and apparent serious or continuing noncompliance per VHA Handbook 1058.01.
- 5) Prompts the PI to report to the NCI CIRB when a regulatory deficiency has been cited on an audit that occurred during the time that the NCI CIRB was responsible for study review.

#### **4. PROCEDURES:**

- 1) Prior to initiating any protocols through NCI CIRB, the PI must have an Annual Principal Investigator Worksheet About Local Context approved by NCI CIRB. The Signatory Institution Primary Contact will review the Annual Principal Investigator worksheet prior to submitting to NCI CIRB. Once this is approved by the NCI CIRB, the PI may submit the Study Specific Worksheet to open a NCI study through NCI CIRB.

#### **TO INITIATE A NEW STUDY**

- 1) The PI submits the Study-Specific Worksheet About Local Context to the NCI CIRB using CTEP site number NC009.
- 2) The Investigator submits required documents to the NCI CIRB and receives study approval.

- 3) The Investigator submits all required forms for PO and ISSO review. This can occur simultaneously with submitting the Study-Specific Worksheet to NCI CIRB.
- 4) The PI submits applicable initial review documents to the research office for local research committee review.
- 5) The initial review submission packet to the local IRB and R&DC will include:
  - a. All NCI CIRB approved study documents to be used locally
  - b. Application for Initial Review—NCI CIRB Protocols
  - c. VA Form 10-0398 Research Protocol Safety Survey
  - d. HIPAA Authorization (VA FORM 10-0493), if applicable
  - e. Request for Waiver of HIPAA Authorization, if applicable
  - f. NCI CIRB approval documentation.
- 6) If Radiation Safety Committee (RSC) review is required, applicable study documents will be provided to RSC. Documentation of Radiation Safety Committee review and approval will be included in the initial review submission packet to DVAHCS research committees.
- 7) The PI delineates in the local research committee initial review submission that the NCI CIRB is the IRB of record for the protocol.
- 8) The PI may start the local committee submission process prior to submission to the NCI CIRB in order to facilitate ancillary committee reviews.
- 9) The PI must receive R&D Committee approval and the Associate Chief of Staff (ACOS) for Research's written notification that all required research committee approvals have been attained, prior to study initiation.

### **REPORTING REQUIREMENTS**

- (1) VA Personnel who become aware of any apparent Local Serious Unanticipated Problems related to the study should report to the DVAHCS IRB and the NCI CIRB Operations Office within five business days of awareness.
- (2) All instances of potential local noncompliance must be reported within 5 working days to the IRB and the NCI CIRB.
- (3) Responses from NCI CIRB related to noncompliance or serious problems should be submitted to the IRB committee.

### **STUDY CLOSE OUTS**

- (1) Studies will be closed with the NCI CIRB using the procedures outlined in the NCI CIRB SOP, as well as with the R&D Committee following the HRPP SOP RR 405.

#### References:

NCI CIRB SOPs  
Durham VAHCS HRPP SOP  
Durham VAHCS R&D SOP  
VHA Directive 1200.05  
VHA Directive 1200.01  
VHA Handbook 1058.01