**LOUIS STOKES CLEVELAND VA MEDICAL CENTER (LSCVAMC)**
**Medical Research Service**
**Standard Operating Policy/Procedure (SOP)**

**Effective Date:** 10/04/2018

**SOP Title:** Use of the National Cancer Institute's Central Institutional Review Board

**SOP Number:** HSP- 001

**Version:** 01

## 1. PURPOSE:

a. To describe the standard operating procedures (SOPs) for the use of the National Cancer Institute's (NCI) Central Institutional Review Board (CIRB) for cancer studies conducted at the LSCVAMC. This SOP is supplemental to the LSCVAMC IRB Policies and Procedures found at: https://www.clevelandvaresearch.com, and the NCI CIRB IRB SOPs found at: https://ncicirb.org/cirb/documents/CIRB_SOPs.pdf.

b. A national Memorandum of Understanding (MOU) is in place between the Veterans Health Administration (VHA) Office of Research and Development (ORD), Office of Research Oversight (ORO), and NCI, Cancer Therapy Evaluation Program (CTEP), CIRB Initiative for human research involving NCI-sponsored cancer research conducted by VA Medical Facilities.

## 2. POLICY:

a. LSCVAMC may rely on the services of the NCI CIRB for review of certain cancer research human studies. Under its Federalwide Assurance (FWA00004231), LSCVAMC is considered to be the Signatory Institution. The LSCVAMC IRB will assist the VA R&D Committee in addressing issues related to the local conduct of research, as outlined below, that are not overseen by the NCI CIRB. The investigators must follow the NCI CIRB guidelines and must also obtain LSCVAMC R&D Committee (R&DC) and applicable local research subcommittee approval to conduct these studies. Oncology studies under the purview of the NCI CIRB at LSCVAMC may not enroll nonveterans, prisoners or children.

b. Neither the local LSCVAMC IRB nor any other IRBs used by LSCVAMC have regulatory jurisdiction over research conducted under the jurisdiction of the NCI CIRB.

## 3. RESPONSIBILITIES:

a. The **Medical Center Director/ Signatory Official** is responsible for:

i. appointing in writing the Signatory Institution Primary Contact (SIPC) to the NCI CIRB;

ii. reporting unanticipated problems, serious and/or continuing noncompliance, local deaths and other serious adverse events, termination or suspension of research, and privacy or information security incidents related to VA research, and other events originating at LSCVAMC as required by VHA Handbook 1058.01 to the Office of Research Oversight (ORO) and external federal agencies or oversight bodies;

iii. updating and signing the FWA and VA Addendum; and

iv. signing the Authorization Agreement/Division of Responsibilities between the VAMC and the NCI CIRB. Copies of the initial signed agreement and all renewals will be sent to the VHA Office of Research Oversight (ORO).

b. The **ACOS/R&D** is responsible for:

i. In addition to the responsibilities outlined in the LSCVAMC R&DC Medical Center Policy, the ACOS/R reviews the proposed application, and determines on behalf of the R&DC whether a study under purview of NCI CIRB should be conducted at LSCVAMC prior to submission of the application to the NCI CIRB.

c. The **R&D Administration Office** is responsible for:

i. ensuring NCI CIRB requirements for enrollment of the Institution and submission of local context forms are met. Completing and submitting the Annual Signatory Institution Worksheet About Local Context, and any other worksheets/forms required by the NCI CIRB for participation;

ii. providing boilerplate language agreed upon by the NCI CIRB and VHA that will be common to all VA research, and, with the PI, resolving concerns related to local study-specific language with the NCI CIRB;

iii. managing evaluation of financial conflict of interest;

iv. receiving correspondence on project approvals, renewals, and determinations from NCI CIRB;

v. notifying the R&DC when a LSCVAMC Principal Investigator (PI) replacement is necessary;

vi. tracking and maintaining all required study related documents in the R&D protocol tracking system;

vii. If the study involves pregnant women, advising the R&DC that the proposed research meets the requirements of 45 CFR 46.204, VHA Handbook 1200.05 par 17, and the ORD guidance on the conduct of such research. The R&D

Administration Office will ensure the facility Director Certification for inclusion of this vulnerable population has been completed Should a subject become pregnant while undergoing treatment in a research study, R&D Administration Office will notify the NCI CIRB for IRB review.

viii. releasing the renewed stamped study documents (informed consent and HIPAA authorization) once the continuing review approval is received from NCI CIRB;

ix. notifying the ACOS/R&D, R&DC, and Institutional Official (IO) of any determinations regarding event reports received from NCI CIRB involving LSCVAMC.

d. The **R&D Committee** is responsible for:

i. overseeing the conduct of the research, monitoring protocol compliance, ensuring that reporting occurs to the NCI CIRB, and ensuring that reporting occurs by the responsible officials to ORO, the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA) and sponsors as required;

ii. providing a mechanism to receive and address concerns from local study subjects and others about the conduct of the research;

iii. ensuring 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;

iv. conducting annual review of the NCI CIRB as part of an annual quality assurance review of the Human Research Protection Program (HRPP), which may include any annual self-assessment completed by the NCI CIRB;

v. reviewing the Study-Specific Worksheet About Local Context to open a study as part of the PO/ISO/Research Office review process;

vi. investigating, managing, reporting and providing any necessary or remedial action to the NCI CIRB per their requirements of any study-specific incidents, experiences, or outcomes regarding any reportable incidents in the timeframes defined by VHA Handbook 1058.01; via the methods specified by the NCI CIRB.

vii. ensuring nonveterans, prisoners, and children are excluded from enrollment in NCI CIRB approved studies;

viii. determining if flags are needed within CPRS for study participants;

ix. ensuring the Information Security Officer (ISO) and Privacy Officer (PO) review is complete prior to study approval;

x. providing final approval to the ACOS/R&D for all initial reviews; and

xi. acknowledging notification of NCI CIRB study closures, reviews of serious adverse events, unanticipated problems and any other items requiring R&DC oversight of the remediation or resolution of the item.

e. The **LSCVAMC IRB** is responsible for:

i. Assisting the R&DC with oversight of institutional requirements that are not overseen by the NCI CIRB;

ii. reviewing and approving requests for waivers of informed consent requirements (if not waived by NCI CIRB) and Health Insurance Portability and Accountability Act (HIPAA) waivers of authorization needed for subject recruitment and ensure that the investigator has made the correct determination about whether a HIPAA Authorization or a Waiver of Authorization is required.

iii. Conducting full board review of any study enrolling prisoners (with a waiver by the CRADO), since the NCI CIRB is not constituted to review studies enrolling prisoners. Note: Prisoners would never be the focus of a NCI study. So, this would only be an issue if a participant became incarcerated during the study. However, it is difficult to continue therapy when a participant is incarcerated due to prison rules. Thus, in most cases, the participant would need to be withdrawn from the study.

iv. If the study will enroll subjects lacking decisional capacity, determining that the conditions for enrollment have been met (see VHA Handbook 1200.05 par 20).

f. The **PI** is responsible for:

i. completing and submitting the Annual Investigator Worksheet about Local Context, the Study-specific Worksheet about Local Context, the Proposed Project Questionnaire (PPQ), and any other relevant documents, to the LSCVAMC R&D Administration Office;

ii. incorporating NCI CIRB-approved boilerplate language into the NCI CIRB-approved model consent form to create the consent form to use for a specific study;

iii. developing a recruitment plan, which includes, when applicable, a waiver of Consent and HIPAA authorization for screening/recruitment approved by the LSCVAMC IRB;

iv. maintaining a regulatory documents file for each study under NCI CIRB purview;

v. providing timely notification of NCI CIRB approval of staff changes to the LSCVAMC SIPC whenever a LSCVAMC Principal Investigator is replaced, or study personnel are added or removed

vi. maintaining compliance with state, local, or institutional requirements related to the protection of human subjects;

vii. notifying the LSCVAMC SIPC if a subject becomes incarcerated or pregnant during participation in a study;

viii. developing a study-appropriate plan for determining (and, as applicable, monitoring) decisional capacity;

ix. forwarding all applicable continuing review and any other event review materials to the LSCVAMC SIPC once uploaded by NCI CIRB;

x. reporting to the NCI CIRB all reportable events and/or incidents as defined and required by VHA Handbook 1058.01;

xi. reporting to the LSCVAMC R&DC or SIPC any reportable incidents as defined by VHA Handbook 1058.01; and

xii. proposing/preparing a management/remediation plan, with advice from the ACOS/R&D if necessary, for local unanticipated problems and serious or continuing noncompliance for R&DC review.

g. The **LSCVAMC** Signatory Institution Primary Contact (SIPC) is responsible for:

i. acting as the institutional designee to receive all NCI CIRB notifications that are communicated to LSCVAMC researchers;

ii. maintaining LSCVAMC NCI CIRB study files;

iii. administrative review of initial and ongoing qualifications of investigators and research staff;

iv. as needed forwarding appropriate study documents to LSCVAMC IRB for review and approval;

v. assuring studies are reviewed as necessary by the PO and ISO and documenting the results of those reviews;

vi. processing study personnel changes;

vii. submitting initial and continuing review approvals to the LSCVAMC R&DC;

viii. sending lapse notices to the PI following notification from the NCI CIRB of the lapse;

ix. processing requests for study closure;

x. responding to requests for consultation, (i.e. questions regarding IRB policies and procedures, etc.) from investigators, research staff, clinicians, etc., IRB members and/or Chairs;

xi. submitting NCI CIRB minutes to R&DC for review and approval.

xii. receiving copies of any NCI CIRB determinations (local or remote) that must be reported by the NCI CIRB to federal regulatory agencies.

h. The **Research Compliance Officer (RCO)** is responsible for:

i. Please refer to MCM 151-019 for details regarding RCO responsibilities.

ii. Conducts audits to ensure compliance with applicable federal, VA and local policy.

iii. 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.

iv. The report to the NCI CIRB is sent by the Signatory Institution Principal Investigator (PI) per NCI CIRB SOPs.

v. Submits audit reports to the R&D Committee. Note: According to the Authorizing Agreement, the NCI CIRB does not oversee the conduct of the study. Therefore, the audit reports with no immediate findings do not need to be sent to the NCI CIRB. Only apparent unanticipated problems and/or apparent serious or continuing noncompliance should be submitted to NCI CIRB by the PI.

## 4. PROCEDURES

a. Prior to initiating any study, the PI must complete the Annual Investigator Worksheet About Local Context and submit it to the ACOS/R&D for review. Once the ACOS/R&D has completed the review and responded to the PI, the PI will then submit the form for review by the NCI CIRB. Following approval of the NCI CIRB, the PI may begin submitting consideration for specific research studies to the appropriate local oversight committees following LSCVAMC standard new study submission process.

b. Initiating a request for LSCVAMC site consideration for studies overseen by the

NCI CIRB:

i. The PI will submit the Request to Review Research Proposal (RRRP), Study-specific Worksheet about Local Context, and any other relevant documents as prompted on the RRRP, to the ACOS/R&D through the R&D Administration Office for review and consideration.

ii. The ACOS/R&D will review the submission and determine if the study should be conducted at the LSCVAMC. The ACOS/R&D will communicate the determination to the LSCVAMC Liaison, who will then coordinate the submission of the package to the NCI CIRB with the PI.

iii. The PI submits the Study-Specific Worksheet About Local Context to the NCI CIRB using the local CTEP site number.

iv. The PI determines if the study team has access to the NCI CIRB Participant Area. If they do not, the PI will contact the LSCVAMC SIPC to request access to NCI CIRB Participant Area. If they do, the PI will contact the LSCVAMC SIPC to request guidance for modified initial submission to the NCI CIRB.

v. The PI submits required documents to the NCI CIRB for review.

vi. The PI receives the approval letter as well as the approved informed consent and HIPAA authorization documents.

vii. The PI submits appropriate study documents, including the approved informed consent and HIPAA authorization documents, to the LSCVAMC SIPC, who forwards the documents to the LSCVAMC IRB for review and determination on issues under their purview (to include waivers of HIPAA authorization and informed consent for recruitment, situations involving prisoners for which the regulations require IRB review, and inclusion of subjects lacking decisional capacity).

viii. The LSCVAMC SIPC ensures studies are reviewed, as necessary, by the Privacy Officer (PO) and Information Security Officer (ISO), and documents the results of the reviews conducted by the PO and ISO.

ix. The LSCVAMC SIPC confirms completed VA credentialing and training for listed study personnel.

x. The LSCVAMC SIPC will submit NCI CIRB initial review approvals to the R&DC once all requirements have been met by applicable subcommittees.

xi. The R&DC reviews the study documents, including the Study-Specific Worksheet About Local Context.

xii. The LSCVAMC SIPC submits NCI CIRB minutes to R&DC for review and approval.

xiii. The LSCVAMC SIPC will note in the Research protocol tracking system that the NCI CIRB is the IRB of record.

xiv. The LSCVAMC SIPC will send the R&DC approval and ACOS notification letter to the PI once final approval is received from the RD&C. The PI may only initiate studies following approval by the R&DC and notification by the ACOS.

c. **Continuing review/Amendments**

i. Studies that require a modification/amendment must be submitted as outlined by the NCI CIRB SOP. After NCI CIRB approval, the amendment/modification will be communicated to the R&DC by the LSCVAMC SIPC.

ii. The PI will submit all required documents to the NCI CIRB for review once prompted by the NCI CIRB.

iii. The LSCVAMC SIPC processes study personnel changes and confirms completed VA credentialing prior to submitting the change to the NCI CIRB.

iv. The LSCVAMC SIPC will receive NCI CIRB continuing review approvals, as well as amendment and other event approvals.

d. **Reporting**

i. Local unanticipated problems must be reported to the NCI CIRB Operations Office within five business days of awareness.

ii. Local apparent serious or continuing noncompliance must be reported to the NCI CIRB within five business days of awareness. 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.

iii. Local deaths and other serious adverse events, termination or suspension of research, and privacy or information security incidents related to VA research must be reported to the R&DC within five business days of awareness.

iv. The LSCVAMC R&DC will provide a plan to manage the incident, experience, or outcome, including measures to prevent similar occurrences when notifying the NCI CIRB of a potential unanticipated problem and/or serious or continuing noncompliance.

v. The LSCVAMC SIPC will receive copies of any NCI CIRB determinations (local or remote) that must be reported by the NCI CIRB to federal regulatory agencies.

vi. The LSCVAMC SIPC will ensure 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;

e. **Study Closure**

i. The PI or NCI CIRB will notify the LSCVAMC SIPC regarding study closure.

ii. The LSCVAMC SIPC notifies the R&DC Coordinator for addition to agenda.

iii. Studies will be closed with the NCI CIRB using the procedures outlined in the NCI CIRB SOP. In addition, the study will be closed at LSCVAMC by the PI notifying the R&DC according to the LSCVAMC study closeout procedures.

**5. REFERENCES:**

a. VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research (http://vaww.va.gov/vhapublications/publications.cfm?Mode=CURRENT&pub=2&order=asc&orderby=pub_Number)

b. Checklist for VAs establishing an Authorization Agreement with the NCI Central IRB (https://vaww.vha.vaco.portal.va.gov/sites/comm/admin/projects/ncicirb/default.aspx)

c. NCI CIRB website (https://www.ncicirb.org/)

**6. RESCISSION:** No previous versions to rescind. Review date for this policy is October 3, 2021

**7. FOLLOW-UP RESPONSIBILITY:** ACOS/R&D