Policy Number: 4
Title: Offsite Research, Cooperative Research and Research at UCI-affiliated Institutions
Date of Last Revision: 10/12/07, 11/06/10, 05/01/16, 08/02/19, 09/23/19, 03/11/20, 06/22/20, 10/12/20, 01/21/22, 09/12/22, 05/11/23

Policy:

I. All human subjects research, including off-site research, cooperative research studies and research at University of California, Irvine (UCI)-affiliated institutions, must be reviewed and approved by UCI's Institutional Review Board (IRB), an independent IRB or other non-UCI IRB as prospectively agreed upon by the UCI IRB or otherwise registered with the UCI IRB, prior to initiation of the research if it satisfies any of the following criteria:
   A. The research is conducted by or under the direction of any UCI employee (i.e., faculty, staff, or student[1]) or agent in connection with his/her institutional responsibilities;
   B. The research uses UCI property, facilities, or resources to support or carry out the activity;
   C. The name of the University of California, Irvine is used in applying for funds (intra or extramural);
   D. The name of the University of California, Irvine is used in explanations and/or representations to subjects;
   E. The UCI employee or agent plans to use their University of California, Irvine association in any dissemination, publication or public presentation resulting from the research;
   F. The research involves the use of non-public information maintained by UCI to identify or contact human subjects or prospective subjects;
   G. UCI receives a direct Federal award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator; and/or
   H. The research is conducted in accordance with an Assurance filed with OHRP in which UCI's IRB is designated as the IRB of record through an established Memorandum of Understanding (MOU).

II. **Memorandum of Understanding (MOU) with Other UC Campuses**
   UCI IRB Committees along with IRB Committees at the other UC campuses and UC-managed laboratories have signed a MOU that allows one UC IRB to rely on another UC IRB for review and approval of human-subjects research protocols that are:
   A. Eligible for expedited review or greater than minimal risk to the subjects and
   B. Will be conducted concurrently at one or more UC location, or
      1. Involves personally identifiable data or samples from one or more UC location for which investigators at another UC location will be conducting analyses.
      2. The MOU, effective March 21, 2006, is reviewed annually to

[1] See HRPP Policy # 12 for exceptions.

determine whether improvements or amendments to the MOU are needed.

C. For studies where UCI is the prime awardee for extramural funding, UCI will serve as the UC Reviewing IRB for the other UC campuses.

D. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

III. **Children's Hospital of Orange County (CHOFC)-Memorial Healthcare Systems (MHS)-UCI (CMU) Agreement for Research**

UCI IRB Committees, CHOC, and MHS have signed an agreement that allows the UCI IRB to rely on the CHOC IRBs for review and approval of human subjects research protocols conducted by UCI researcher (i.e., faculty, staff, or student) that are solely conducted at CHOC. One exception to this provision is when a UCI researcher submits a positive COI Disclosure requiring a UCI COIOC management plan. In this instance, UCI IRB review and oversight is required. Other exceptions shall be determined by the Institutional Official at either UCI, CHOC, or MHS.

A. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

IV. **SMART IRB** - the "Streamlined, Multisite, Accelerated Resources for Trials" IRB Reliance platform supported by the National Center for Advancing Translational Sciences (NCATS) to facilitate multi-site clinical trials.

A. **Important note**: SMART IRB is not an actual IRB that provides regulatory approval. SMART IRB provides a roadmap for institutions to implement the Single IRB Review requirements. Through a flexible master IRB reliance agreement, standard operating procedures, and complementary tools and resources, SMART IRB supports and encourages collaboration and harmonization across the nation.

B. **In an effort to promote a more streamlined process, where UCI serves as the IRB of record, UCI will utilize the SMART IRB agreement instead of the UC IRB Reliance or MOU. A Letter of Agreement between both institutions is required.**

V. **Fountain Valley Regional Hospital -** UCI has also entered into an MOU wherein UCI serves as the IRB of Record for Fountain Valley Regional Hospital. UCI will also act as its HIPAA Privacy Board.

VI. **Memorandum of Understanding (MOU) with the National Cancer Institute (NCI) Central Institutional Review Boards (CIRBs)**

A. UCI IRB Committees have established an MOU with the NCI Adult and Pediatric CIRBs. The MOU allows the UCI Committees to rely upon the NCI CIRB for:

1. Review of Cooperative Group Trials from the following cooperative groups: ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC, NSABP, RTOG, and SWOG, as well as any other studies opened in the Cancer Trials Support Unit.

VII. **UCI has also entered into MOUs where a non-UCI IRB is designated as the IRB of Record for example:**

A. National Cancer Institute Central IRB (CIRB) for review and oversight of NCI multi-center, adult cooperative oncology studies.

B. StrokeNet Central IRB for review and oversight of small and large clinical trials and research studies to advance acute stroke treatment, stroke prevention, and recovery and rehabilitation following a stroke.

C. NeuroNEXT, or Network for Excellence in Neuroscience Clinical Trials, was created to conduct studies of treatments for neurological diseases through partnerships with academia, private foundations, and industry.

D. NEALS, or Northeast Amyotrophic Lateral Sclerosis (ALS), is a non-profit group of research institutions who collaboratively conduct clinical research in ALS and other motor neuron diseases.

E. Independent IRBs for review and oversight of industry-authored clinical trials, including:
   1. Western IRB (WIRB) or its affiliates;
   2. Advarra

F. UCI continues to enter into IRB Authorization Agreements and MOUs to support single IRB review of multi-site trials and cooperative research.

VIII. **UCI IRB as the IRB of Record or Coordinating Center for Multi-site Research**

The UCI IRB will serve as the IRB of Record for an offsite location when the offsite location is engaged in human research.

A. **Differences between "IRB of Record" and "Coordinating Center."**
   1. When the UCI IRB serves as the IRB of Record, it is accepting the responsibility of research conduct oversight for a particular study or site. The details of such an agreement are outlined in a Memorandum of Understanding, as necessary.
   2. When UCI serves as the Coordinating Center (i.e., the UCI investigator is the lead investigator of a multi-site study or UCI is the lead institution of a multi-site study), the UCI investigator is responsible for assuring that IRB approval is granted at the participating sites prior to the initiation of the research at that site. It is important to note that even when UCI serves as the "Coordinating Center," the UCI IRB is not serving as the IRB of Record for all sites. The Coordinating Center assumes responsibility for assuring that the participating site(s) has received IRB approval.
   3. Under rare circumstances, the UCI IRB may be requested to serve as the IRB of Record for a participating site of a multi-center trial in which a UCI Investigator is serving as the "Coordinating Center." The participating site either may not have an IRB, or due to other circumstances, may request the UCI IRB to serve as their IRB of Record for that particular study at that particular site.

B. **UCI IRB as the IRB of Record**

1. The Senior Director of Human Research Protections (HRP), the Director of HRP or designee, including the IRB Chair/s or IRB Vice Chair/s, the Associate Vice Chancellor, or the Institutional Official will make all final determinations regarding the UCI IRB Committee's willingness to serve as the IRB of Record and Privacy Board for an offsite location "engaged" in research.
2. A Memorandum of Understanding (MOU) is executed when the UCI IRB serves as the IRB of Record for a site that is not a UCI-affiliated site. The MOU outlines specific provisions and responsibilities for each party entering into the agreement. The OHRP IRB Authorization template is one example of a MOU that may be used.
3. The UCI IRB will not accept an "Unaffiliated Investigator Agreement" in order to serve as the IRB of Record. All agreements for the UCI IRB to serve as the IRB of Record for a performance site "engaged" in research must be detailed in a MOU and an executed agreement negotiated by UCI Sponsored Projects when federal funds are involved.
4. Conditions for the UCI IRB to serve as the IRB of Record:
    a. UCI investigator will be conducting research at the offsite institution. The institution engaged in human research does not have an IRB and will rely solely on the UCI IRB for review of human subjects research activities; *or*
    b. The performance site engaged in human research may or may not have an IRB of Record but will rely on the UCI IRB for a specific research project.
    c. The research shall be conducted in collaboration with UCI; and
    d. The UCI Investigator has a formal affiliation with UCI.
    e. In general, the relying institution is not an international site.
5. When federal funds are involved, the performance site engaged in research requesting UCI IRB to serve as the IRB of Record must:
    a. File a Federalwide Assurance (FWA); and
    b. Conduct the research in accordance with the terms and conditions specified in the executed agreement negotiated by UCI Sponsored Projects.
6. The UCI investigator must provide all necessary information pertaining to local research activities conducted at an offsite location in the UCI IRB protocol and in accordance with UCI IRB policies and procedures.
7. The UCI IRB and offsite location will maintain an approved Federalwide Assurance (FWA) and provide verification of such during the negotiation of the MOU.
8. Investigators will comply with all oversight activities deemed appropriate by the UCI IRB, Federal oversight agencies and/or Federal funding agencies at all sites (e.g., monitoring, auditing).
9. **As noted above, where a cooperative institution has an IRB and UCI is requested to serve as the IRB of record, UCI will require the use of the SMART IRB.**

10. **Requests for collaborating sites to rely on the UCI IRB must be made via a formal amendment to the UCI IRB approved study. Reliance agreements where UCI serves as the IRB of record will not be considered at initial review due to the amount of time involved as this often protracts the initial IRB approval timeframe for the UCI site.**
11. **Regarding HIPAA: When collaborative sites have their own Privacy Board, the UCI IRB (which serves as the Privacy Board at UCI) will not serve as the Privacy Board for the relying institution.**

C. **Communication with other IRBs**

1. **The UCI investigator must provide all necessary information regarding local contact information in the UCI IRB application.**
2. The UCI investigator or representative from the offsite location must provide to the IRB and keep current the names, addresses, and phone numbers of local contact persons who can make decisions regarding IRB issues.
3. UCI requires that the offsite location, relying on the UCI IRB as the IRB of Record, communicate any audit findings or other problems associated with the conduct of research to UCI IRB. Findings or problems include but are not limited to: unanticipated problems involving risk to participants or others, complaints from research participants, or any serious or continuing non-compliance issues.
4. The UCI IRB will report promptly to the appropriate institutional officials of the offsite location all actions taken by the UCI IRB regarding (a) any serious or continuing noncompliance by investigators and (b) any suspension or termination of IRB approval in accordance with the UCI IRB policies and procedures.

D. **Coordinating Center for Multi-site Research**

1. The UCI investigator must provide all necessary information regarding participating sites in the UCI IRB application.
2. The UCI IRB will acknowledge the existence of any Coordinating Center established or affiliated with a UCI investigator and determine whether the Coordinating Center has sufficient mechanisms in place for the protection of research participants when acting as a Coordinating Center.
3. The UCI IRB must determine that the UCI Coordinating Center has sufficient mechanisms in place to assure that:
    a. An adequate plan is in place to address project management and data and safety monitoring given the nature of the research.
    b. IRB approval at the participating sites will be obtained prior to initiation of the research at that site (the UCI investigator is responsible for obtaining each site's IRB approval letter and IRB approved informed consent documentation);
    c. UCI IRB approval will be obtained before implementing any changes to the UCI IRB-approved study, and IRB approval will be obtained at the participating sites before implementing modifications at the sites.

d. Participating sites have a mechanism for reporting interim results.
e. The participating sites have written procedures for assuring prompt reporting to the UCI IRB of any unanticipated problems involving risk to participants or others; any serious or continuing non-compliance; and any suspension or termination of IRB approval for cause.
f. In addition, each site is responsible for reporting any unanticipated problems involving risk to participants or others; any serious or continuing non-compliance; and any suspension or termination of IRB approval for cause directly to OHRP, the FDA, as applicable.

IX. UCI IRB as the Relying IRB

A. The Senior Director of Human Research Protections (HRP), the Director of HRP or designee, including the IRB Chair/s or IRB Vice Chair/s, the Associate Vice Chancellor, or the Institutional Official will make all final determinations regarding the UCI IRB Committee's willingness to rely on a non-UCI IRB.
B. UCI will maintain the responsibility of the Privacy Board for matters relating to UCI HIPAA.
C. In general, UCI may rely upon the IRB of another institution provided one of the following is true:
    1. The IRB is the IRB of an AAHRPP accredited organization, or the organization is actively seeking AAHRPP accreditation.
    2. The IRB has current certification from the Consortium for Applied Research Ethics Quality (CARE-Q).
    3. The UCI Investigator is a collaborator on human research primarily conducted at another institution and the UCI investigator's role does not include interaction or intervention with subjects.
    4. UCI is engaged in human research solely because UCI is the prime awardee. UCI investigators will not interact or intervene with subjects or collect or possess private identifiable information about subjects, nor obtain informed consent.
    5. Unless it is an IRB Organization, the institution must maintain an OHRP-approved Federalwide Assurance ("FWA"), regardless of whether it engages in federally funded human subjects research that is subject to the Federal Policy for the Protection of Human Subjects ("Federal Policy").
        a. **If the reviewing institution is not signed on to the SMART IRB (requiring the above), evidence of the FWA is to be verified by HRP Staff.**
    6. An executed Memorandum of Understanding (MOU) will be executed. The MOU will outline the specific provisions and responsibilities for each party entering into the agreement.

X. Department of Defense (DoD) Research

A. When UCI IRB is relying, the relying IRB will address requirements as per the DoD Instruction (DoDi) 3216. 02.
B. **Department of Navy (DoN) Research:**
    1. DoN commands and activities may collaborate with each other, other DoD agencies, non-defense federal agencies and non-

federal institutions. An appropriate written agreement shall be established between the collaborators that includes a Statement of Work (SOW) and specific assignment of responsibilities.

a. The agreement should briefly describe the research, specific roles and responsibilities of each institution, responsibility for scientific and IRB review, recruitment of subjects, and procedures for obtaining informed consent. The agreement also should describe provisions for oversight and ongoing monitoring, reporting requirements, documentation retention and compliance for the entire research project. All collaborators must ensure compliance with all relevant human subject protection regulations at their sites. Collaborating institutions that rely on other institutions' IRBs for human subject protections to avoid duplication of effort must ensure that such reliance does not compromise any standards of requirements.

References:

21 CFR 50.3(c)
45 CFR 46.102 (d, f)
California Health and Safety Codes 102231, 125115-125117
UCI Research Policy for the Protections of Human Subjects in Research
SECNAVINST 3900.39D 8f
DoDi 3216.02

Procedure Number: 4.A

Title: Procedure for Review of UC MOU Multi-campus Research

Procedure:

MOU with other UC Campuses: This procedure describes the process for review of protocols under the UC MOU for multi-campus research studies.

I. **When the UCI IRB is Relying on Another UC Campus:**

- A. The UCI investigator notifies the UCI IRB and the UC reviewing IRB of the intent to submit a protocol under the UC MOU via the IRB Application.
- B. The UCI IRB will determine if reliance upon another UC campus for IRB review is acceptable. Also, the reviewing IRB has to agree to perform the review. The UCI IRB and/or the reviewing IRB will notify the UCI investigator by e-mail or phone if there is a problem.
- C. UCI will maintain the responsibility of the Privacy Board for matters relating to UCI HIPAA.
- D. UCI will maintain consent template injury language, as applicable in the UCI consent form/ document.
- E. The UCI IRB will issue an Administrative Registration letter to the UCI investigator and the Reviewing IRB. The registration period will coincide with the reviewing IRB approval expiration date. The UCI investigator must keep a copy of the registration letter and approval documents for their records.

II. **When the UCI IRB is Reviewing for Another UC Campus:**

- A. UCI will require the use of the SMART IRB to facilitate multisite research.
- B. The UCI IRB will determine if reliance upon another UC campus for IRB review is acceptable. In addition, the reviewing IRB has to agree to rely.
  1. When UCI requests that UC Berkeley rely, HRP Staff will reach out to the UC Berkeley IRB Director to confirm prior to moving forward with the reliance.
- C. UCI will not serve as the Privacy Board for non-UCI sites.
- D. The UCI IRB will issue an IRB Approval letter to the UCI investigator.
- E. The UCI investigator must keep a copy of the registration letter and approval documents for their records.
- F. **Further, the UCI investigator is responsible for forwarding all UCI IRB approval documents to the non-UCI site.**

III. **UCI Lead Researcher (LR) Responsibilities**

- A. <u>UCI Investigator Responsibilities to UC Reviewing Campus</u>: The UCI Investigator must comply with all decisions of the reviewing IRB. This includes following the standards and guidelines of the reviewing IRB for the reporting of any unanticipated problem involving risk to participants or others and other safety information.
- B. <u>UCI Investigator Responsibilities to the UCI IRB</u>: The UCI Investigator is responsible for advising the UCI IRB of any amendments or continuation of the approved study by submitting copies of such materials to the Office of Research Administration.
- C. <u>Preserving Efficiencies at UCI:</u> Where efficiencies are in place at UCI to reduce researcher burden, such as the use of the Study Team Tracking Log for the addition and removal of Research Personnel, UCI researchers

may continue to utilize such efficiencies. The UCI Investigator should first confirm such practice would not be in conflict with the requirements of the reviewing IRB, as appropriate.

IV. **Non-UCI LR Responsibilities**

A. UC Relying Campus Investigator Responsibilities: Investigators should contact their IRBs for details on the acknowledgment process for their campus.

V. **IRB Analyst or Higher Responsibilities**

A. When a request to rely on another UC IRB is received, prepares materials for IRB review to determine if reliance on another UC IRB is acceptable.
B. Prepares correspondence requesting revisions from the IRB and approval letters using the appropriate template.
C. Assures all appropriate database entries are completed.
D. Assures all relying campuses receive UCI IRB acceptance or approval documentation.

Procedure Number 4.B
Title: Procedure for Review of NCI CIRB Approved Studies

Procedure:
This procedure describes the process for review of NCI CIRB-approved studies by the UCI IRB Committees.

I. **Background**

The Central Institutional Review Board (CIRB) Initiative is sponsored by the National Cancer Institute (NCI) in consultation with the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP). The CIRB provides expert IRB review at the national level before the Cooperative Group distributes the protocol to local investigators. The CIRB is composed of individuals who represent a broad range of oncology disciplines and may include oncology physicians, nurses, patient representatives, pharmacists, ethicists and attorneys. Because UCI has established a formal agreement with the NCI CIRB, investigators who wish to participate in the Cooperative Group Trials reviewed by the NCI CIRB may take advantage of these reviews.

The CIRB currently reviews Cooperative Group Trials from the following cooperative groups: ACOSOG, CALGB, ECOG, GOG, NCCTG, NCIC, NSABP, RTOG, and SWOG, as well as any other studies opened in the Cancer Trials Support Unit.

II. **NCI CIRB Review Procedures**

A. The established national cooperative research groups are charged with designing and evaluating protocols related to specific disease types. The cooperative groups forward to the NCI CIRB the protocol, the informed consent document(s), a completed CIRB application and, when appropriate, an investigator drug brochure via the Protocol Information Office at NCI.

B. The CIRB members meet at least once a month. At the meetings the Board members discuss the protocol and may consult by telephone with the Study Chair to explore any concerns they may have.

C. The Board takes one of the following actions for each protocol: approve, approve pending modification, table, or disapprove. Any non-approval is followed up with communication with the Study Chair to resolve, wherever possible, outstanding issues identified by the Board.

D. After approval or disapproval, the Study Chair and Cooperative Group sponsor are formally notified.

E. For each protocol, the CIRB's primary reviews, minutes, notification letters, and any other correspondence are posted in a section of NCI CIRB for participating institution’s IRBs to access.

F. In addition to conducting initial reviews, the CIRB conducts Continuing Reviews and reviews of Serious Adverse Events (SAEs), Data Safety Monitoring Board (DSMB) reports, protocol amendments, national subject recruiting materials, etc. These actions are also posted on the web site for prompt access by participating institutions.

III. **Lead Researcher (LR) Responsibilities**

A. The single IRB (sIRB) Application for CIRB studies must be accompanied by the Local IRB Facilitated Review Packet available on the NCI CIRB website.

B. The sIRB Application for CIRB studies is brief and is designed to capture information about the local context (e.g., study team, recruitment and informed consent processes, reporting of any unanticipated problem involving risk to participants or others and confidentiality of data).

C. In addition to completing the sIRB Application, the NCI CIRB consent must include specific UCI template language additions.

D. The following information must be included with the sIRB Application:

1. The Local IRB Facilitated Review Packet from the “Participant side” of the NCI CIRB website.
2. An informed consent document that conforms to the UCI consent template.

E. LRs must review the CIRB website regularly to keep current with all information including amendments to CIRB-approved studies. UCI requires facilitated review of study amendments.

F. LRs must track study expiration dates to prevent study approvals from expiring. UCI requires facilitated review of continuing renewals.

G. LRs must submit any internal (on-site) unanticipated problem involving risk to participants or others to both the UCI IRB and the NCI CIRB.

H. LRs must submit renewal and modification materials to both UCI and CIRB in a timely manner so that approvals and facilitated reviews may be kept in synch.

IV. **UCI IRB Review Procedures:**

A. A subcommittee of the IRB will conduct a "facilitated review" of the study submitted by the UCI investigator. The subcommittee is usually the IRB Chair, Vice Chair or another voting member with sufficient oncology expertise. The subcommittee reviews the submission and any other materials available on the CIRB web site (e.g., minutes), so they can determine whether there are local concerns that need to be addressed and whether to accept the CIRB Review.

B. The subcommittee has the authority to accept the CIRB approval "as is," accept it with minor modifications (see Policy # 11) or they may decide not to accept the CIRB review and require that the investigator submit a protocol for full committee review (see Policy # 14). If the subcommittee does not accept the CIRB review they may still utilize CIRB written materials as resources for full committee review.

C. The subcommittee has authority to require and approve additions to the informed consent. UCI template language must be added to the informed consent dealing with institutional requirements and IRB policies. *No CIRB approved information may be deleted from the informed consent document***.** The IRB may also make minor word substitutions or additions in the informed consent document, particularly to facilitate better comprehension by the local population, as long as the proposed changes do not alter the meaning of the CIRB approved contents. Additional risks may be added to the informed consent document. NOTE: Revisions/changes to the UCI consent form other than those described above require full committee review. In this instance, facilitated review will not be used and the CIRB will not serve as the IRB of record for the protocol at UCI.

D. Once approved, the UCI IRB sends a CIRB approval notice to the investigator. The date of protocol expiration is set to the expiration date of the CIRB approval. Example: the CIRB study expiration date is April 20, 2007. UCI accepts CIRB approval on June 10, 2007. The UCI approval period for the study would be June 10, 2007 to April 20, 2008.

E. The UCI HRP office will notify the CIRB Administrative Office each time it accepts the CIRB review of a protocol, by clicking on the "Facilitated Review Acceptance" link within the main menu for each protocol and completing the Facilitated Review Acceptance Form. In order for the CIRB to become the Official IRB of Record for the site for a particular study, this form needs to be completed and submitted online. A separate form must be submitted for each protocol review that is accepted.

F. The CIRB will use UCI's reply to set up a database both for record keeping and notification purposes. The CIRB will notify the local IRB when there are any actions taken on the protocol, e.g., an SAE report requiring a change in the consent form, an approved protocol amendment, a change in the protocol/informed consent resulting from the Continuing Review, etc.