1 Purpose

This SOP establishes the processes and procedures for ensuring the rights, safety, and welfare of research participants are protected when UNC-Chapel Hill shares responsibility for research oversight with another organization.

2 Policy

All non-exempt human subject research conducted under the auspices of The UNC-Chapel Hill must be reviewed and approved by the UNC-Chapel Hill IRB or another designated IRB prior to the initiation of the research, unless it has been determined that UNC-Chapel Hill is not engaged in the research. The authorized off-site IRBs that serve as the IRB-of-record for UNC-Chapel Hill research have the same authority as the on-site IRBs, and all determinations and findings of the off-site IRBs are equally binding on all research conducted under the auspices of the organization.

In the conduct of cooperative research projects, UNC-Chapel Hill acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. It is the policy of UNC-Chapel Hill to assure that all entities engaged in human subjects research receive adequate documentation about the study in order to protect the safety, welfare and interests of study participants. In the context of cooperative or collaborative human subjects research, UNC-Chapel Hill and the other institutions engaged in the research may choose to conduct concurrent IRB review, unless such review is prohibited by applicable regulations or funding agency policy. Alternatively, UNC-Chapel Hill may enter into a written reliance agreement under which UNC-Chapel Hill relies on the review of another qualified IRB or an external institution relies on the review of the UNC-Chapel Hill IRB.

When UNC-Chapel Hill relies on an external IRB for oversight, or when an external entity relies on the UNC-Chapel Hill IRB for oversight, UNC-Chapel Hill will be responsible for executing a reliance agreement that describes how the responsibilities for protecting human subjects are divided between UNC-Chapel Hill and the non-UNC-Chapel Hill entity. When the research involves federal support and/or funding, an appropriate assurance must be held by the entities party to the agreement. When research is subject to the HHS 2018 Common Rule, UNC-Chapel Hill complies with the requirement to rely on the review of a single IRB for that portion of cooperative research conducted in the United States.

The UNC-Chapel Hill OHRE is responsible for maintaining reliance agreements and associated documentation. When the UNC-Chapel Hill IRB has been designated as the IRB of record, the IRB review process and regulatory oversight will be governed by UNC-Chapel Hill IRB policies.
When UNC-Chapel Hill cedes oversight to an external IRB, the IRB review process and regulatory oversight will be governed by the external IRB’s policies. Reliance agreements must include and address the following:

- Scope of the covered research;
- Providing education to researchers and research staff;
- Conducting scientific review;
- FWA status of the parties;
- Responsibilities for HIPAA determinations related to the covered research;
- IRB independence and authority;
- IRB decisions;
- Compliance responsibilities of the relying entity;
- Reviewing potential non-compliance, including complaints, protocol deviations, and results of audits and making determinations regarding whether each incident of non-compliance is serious or continuing;
- Reporting determinations of non-compliance and unanticipated problems to federal agencies;
- Ensuring disclosure and management of individual investigator conflicts of interest and institutional conflicts of interest;
- Cooperation in investigations and corrective actions;
- Recordkeeping and access to IRB meeting minutes;
- Termination of the relationship and provision for continued oversight of ongoing research; and
- Communications.

The UNC-Chapel Hill OHRE Director or designee has the authority to make decisions regarding whether UNC-Chapel Hill’s IRB will serve as the Reviewing IRB or whether UNC-Chapel Hill will cede review to an external IRB.

3 Procedures

3.1.1 Reliance on External IRBs

The UNC-Chapel Hill may rely on external IRBs for regulatory review of research conducted under the auspices of the university. UNC-Chapel Hill considers the following non-exhaustive list of factors when deciding whether to rely on an external IRB for regulatory review:

- Whether single IRB review is required by the sponsor or applicable regulations or policies;
- UNC-Chapel Hill’s role in the research;
- The risk level of the research;
• Where the research interventions will be performed, and by whom;

• Qualifications and experience of the researchers performing more than minimal risk interventions or procedures; and

• Whether the proposed Reviewing IRB is AAHRPP-accredited.

UNC-Chapel Hill generally only agrees to cede review to external IRBs that are AAHRPP-accredited. The UNC-Chapel Hill OHRE Director or designee may make study-specific exceptions to this requirement if, after reviewing the proposed Reviewing IRB’s policies and procedures, it is determined that the proposed Reviewing IRB’s policies and processes are consistent with ethical standards and applicable regulations.

When UNC-Chapel Hill agrees to rely on an external IRB, the University and the OHRE ensure the following:

• UNC-Chapel Hill researchers comply with the determinations and requirements of the Reviewing IRB, including requirements related to initial and continuing review, record keeping and reporting, and promptly reporting any proposed changes to the research to the Reviewing IRB;

• The Reviewing IRB is provided with requested information about local requirements or Local Considerations relevant to the reviewing IRB’s determination, prior to the regulatory review;

• Notifying the Reviewing IRB when local policies that impact IRB review are updated;

• UNC-Chapel Hill officials shall not approve research subject to a reliance agreement if it has not been approved by the reviewing IRB;

• Researchers shall not enroll participants prior to review and approval by the Reviewing IRB and meeting all UNC-Chapel Hill requirements for conducting the research (e.g., completing all UNC-required ancillary reviews);

• All information requested by the Reviewing IRB is provided in a timely manner;

• Researchers and research staff disclose potential conflicts of interest according to UNC-Chapel Hill policies, comply with any resulting COI management plans and management plans are provided to the Reviewing IRB;

• Reports of non-compliance, participant complaints, protocol deviations, unanticipated problems involving risks to participants or others, data safety monitoring reports, and other events specified in the applicable reliance agreement are promptly reported as specified in such agreement;

• Researchers responsible for enrolling participants obtain, document, and maintain records of consent for each participant or each participant’s legally authorized representative;
• Researchers provide to the reviewing IRB data safety monitoring reports they receive, according to the reviewing IRB’s reporting policy;

• Conduct monitoring in addition to or in cooperation with the reviewing IRB, when appropriate;

• Researchers and research staff have the appropriate qualifications, expertise and training to conduct the proposed research.

3.1.2 Reliance on Commercial IRBs

UNC-Chapel Hill requires the use of a pre-approved Commercial IRB for industry-sponsored, multi-center, clinical research studies, as outlined in SOP 401. Exceptions to this requirement may be granted by the OHRE Director or designee.

Investigator-initiated studies are only eligible for review by Commercial IRBs at the discretion of the OHRE Director or designee.

Investigator Responsibilities

Prior to submitting the application package to a Commercial IRB, the investigator must satisfy the UNC-Chapel Hill application requirements for externally reviewed studies. An abbreviated IRBIS application must be completed in order for the UNC-Chapel Hill IRB to confirm completion of all institutional requirements (e.g., radiation safety review, COI disclosure, applicable training, data security requirements) and for record-keeping purposes.

Per UNC-Chapel Hill agreements with the Commercial IRBs, the Commercial IRB will invoice the Sponsor/CRO directly. UNC charges an additional preparation/processing fee which should be included in the study budget.

The UNC-Chapel Hill Responsibilities:

Following submission of the abbreviated application in IRBIS, UNC-Chapel Hill IRB staff review the following:

• Application for completeness and consistency between sections;

• Eligibility to use external IRB review (industry-sponsored study);

• Investigator and study staff (confirmation of current training and COI disclosure);

• Institutional requirements (e.g., radiation safety, Investigational DrugServices (IDS) pharmacy approval, concurrence of subject injury language in the consent with that approved by the UNC Office of Clinical Trials);

• If applicable, adequacy of justification for limited waiver of HIPAA authorization and HIPAA Authorization form (free-standing, i.e., not embedded into the main consent document) is reviewed for required content.
Once the above are reviewed by the UNC-Chapel Hill IRB and determined to be acceptable, the IRB issues the investigator a Permission to Register/contingency letter and UNC-Chapel Hill study-specific Cover Sheet. The letter permits the investigator to move forward with their submission to the external IRB, while the Cover Sheet provides applicable study specific information, e.g., stand-alone HIPAA authorization information, IRBIS number, sites and results of ancillary reviews including COI disclosure language and other management controls (provided by the Conflict of Interest Office), Radiation Safety Committee review results, and subject injury language concurrence with the clinical trial agreement [CTA] (managed by the Clinical Trials Office). Both COI disclosure/management and subject injury language for Network Entity researchers are managed by the Network Entities Research Compliance office.

Investigator Responsibilities: Post Commercial IRB Approval

Once the investigator has received approval from the Commercial IRB, they must submit the IRB-approved UNC-Chapel Hill site-specific consent document (if any) and the IRB approval letter of the UNC site via IRBIS. The IRB office will review the UNC site-specific consent (if any) to confirm congruency of institutional requirements specified in the Cover Page and shall issue final approval of the rely-on application if the site-specific consent contains all applicable information.

Pursuant to UNC Chapel-Hill’s Authorization Agreements with Commercial IRBs, the Commercial IRB must copy the UNC-Chapel Hill IRB Office on all determinations of continuing or serious non-compliance and unanticipated problems involving subjects or others (UPIRSO) for the UNC-Chapel Hill site. Investigators must report these events to the UNC-Chapel Hill IRB pursuant to requirements of SOP 1401. These will be reviewed by the UNC-Chapel Hill IRB Compliance Office as described in SOP 1402.

The Principal Investigator must “renew” the study annually with the UNC IRB by completing an abbreviated renewal submission that includes submission of the current approved consent forms and current external IRB approval letter. As with all studies, COI disclosures must be completed at least annually by applicable members of the research team.
3.1.3 Reliance on the National Cancer Institute's Central IRB Adult and Pediatrics Initiative

The UNC-Chapel Hill is a participant in the National Cancer Institute’s Central Institutional Review Board (CIRB) Initiative for cooperative group protocols/studies that have been reviewed and approved by the CIRB. The Lineberger Cancer Center Clinical Protocol Office submits the necessary documentation to maintain institutional registration with the CIRB, including the “Authorization Agreement/Division of Responsibilities,” the listing of Key Personnel, and the “Annual Signatory Institution Worksheet About Local Context.”

The CIRB defers responsibility to local institutions to conduct any reviews necessary under HIPAA.

Investigator Responsibilities:
Investigators wishing to use the NCI CIRB must:

1. Contact the Lineberger Comprehensive Cancer Center (LCCC) NCI CIRB Manager to request the materials necessary to register as an investigator with the CIRB.

2. Complete, on an annual basis, the “Annual Principal Investigator Worksheet About Local Context” and submit to the LCCC NCI CIRB Manager and to the CIRB. Once CIRB-approved, the investigator may proceed with individual study applications.

3. In order to submit individual protocols/studies to the CIRB, the investigator must first submit a study-specific application to the UNC-Chapel Hill IRB via IRBIS that includes the following:
   a. Study Summary and Key Personnel,
   b. Abbreviated IRB application,
   c. The protocol/research plan version, investigator brochure(s), and model consent currently approved by the NCI CIRB,
   d. The consent form for local use with required local institutional language incorporated,
   e. Translations of the consent form for local use with accompanying translation verification form, and
   f. HIPAA authorization form.

4. UNC-Chapel Hill IRB staff will review the abbreviated application, facilitate the COI review process, and provide a letter either accepting or declining CIRB oversight of the study (as a component of organizational approval).
   a. If accepted, the investigator may then proceed with the application to the CIRB by submitting the CIRB “Study-Specific Worksheet About Local Context”. Note: If a member of the research team has a COI Management Plan, this must be submitted to the CIRB.
   b. If declined, a reason will be provided and the investigator will be given an opportunity to provide additional or clarifying information. In the event that the
decision to decline is confirmed on re-review, the investigator may appeal the decision by contacting the UNC-Chapel Hill IRB office.

5. Once approved by the CIRB, the UNC-Chapel Hill PI must submit a copy of the CIRB approval letter to the UNC-Chapel Hill IRB Office via IRBIS.

The UNC-Chapel Hill Responsibilities: Post CIRB Approval
The UNC-Chapel Hill is responsible, per written agreement with the CIRB, to ensure compliance with the regulations governing human subjects research and the determinations made by the CIRB, and to report possible serious or continuing non-compliance and unanticipated problems to the CIRB for evaluation. In order to fulfill these responsibilities, the UNC-Chapel Hill needs to maintain current documentation of the study, the actions taken by the CIRB, and any local issues that arise with the research. Annually, the Principal Investigator must submit an administrative review application that includes the following: amended protocols, local consent documents and the most recent NCI CIRB approval letter.

The UNC-Chapel Hill IRB Office staff will review submissions and seek additional information, if needed, from the local research team. The UNC-Chapel Hill IRB Office will report potential unanticipated problems, potential serious or continuing non-compliance, local suspensions or terminations of research activities, and audit reports that note regulatory deficiencies to the CIRB. The report will include, if applicable, a corrective and preventative action plan (CAPA) developed in cooperation with the investigator. The CIRB will make a final determination regarding whether or not such events are unanticipated problems involving risks to subjects or others, serious non-compliance, or continuing non-compliance and will initiate any necessary reporting to sponsors and federal agencies.

3.1.4 Reliance on External Institutional IRBs

UNC-Chapel Hill may rely on the IRB of a collaborating institution. This may be because the majority of the non-exempt human-subjects research is being conducted at the collaborating institution, the collaborating institution’s IRB has more relevant or specialized expertise and/or knowledge of the site where the research will be conducted, or because the collaborating institution has been designated as the sIRB (single IRB). In such cases, a reliance agreement must be executed. The institution relied upon for IRB review must have an active/approved FWA. In the absence of such a reliance arrangement, each institution will independently review the research project.

Investigator Responsibilities
Investigators seeking to rely on the IRB at a collaborating institution must submit a study-specific application to the UNC-Chapel Hill IRB via IRBIS that includes the following:

a. Study Summary and Key Personnel,
b. Abbreviated IRB application,
c. Protocol, investigator’s brochure (as applicable), and consent forms approved by the reviewing IRB,
d. The consent form for local use with required local institutional language incorporated,
e. UNC HIPAA authorization form (as applicable), and
f. A copy of the reviewing IRB’s approval letter and any required
documents for relying sites (e.g. Local Context Form).

The UNC-Chapel Hill Responsibilities
UNC IRB staff will review the application for completeness and determine whether reliance is appropriate based on the factors enumerated within this SOP. If reliance is appropriate, once reliance-related documents (i.e. the reliance agreement and any required relying site documents) have been completed, UNC IRB staff will return the application to the investigator with a stipulation indicating that the study team may proceed with obtaining approval of the UNC site from the reviewing IRB. If reliance is not appropriate, UNC IRB staff will correspond with the study team to provide appropriate guidance on next steps.

Investigator Responsibilities: Post Commercial IRB Approval
After the reviewing IRB has approved UNC as a relying site, the UNC-Chapel Hill investigator will upload the reviewing IRB’s approval letter and UNC site-specific consents (if any) into IRBIS and resubmit the application for final review by UNC IRB staff. UNC IRB staff will conduct a final review of the application and if all UNC requirements have been met, will issue a final approval letter. Research activities may begin at UNC only after the UNC study team has received this final approval letter.

The Principal Investigator must “renew” the study annually with the UNC IRB by completing an abbreviated renewal submission that includes submission of the current approved consent forms and current external IRB approval letter. As with all studies, COI disclosures must be completed at least annually by applicable members of the research team.

3.1.5 UNC-Chapel Hill IRB Serving as the Single IRB:
When the UNC-Chapel Hill serves as the single IRB for Relying Institutions or non-UNC-Chapel Hill individual investigators, UNC-Chapel Hill will ensure that the structure and composition of the IRB is appropriate to the research reviewed and complies with applicable laws. This shall include ensuring that the UNC-Chapel Hill IRB is properly constituted, that members are appropriately qualified, that members do not participate in the review of studies with which they have a conflict of interest, and that the IRB follows policies to separate business functions from the ethical review.

Investigator Responsibilities
UNC-Chapel Hill investigators seeking to have the UNC-Chapel Hill IRB serve as the single IRB may request a Letter of Support to include in a grant proposal. Investigators may also submit an application in IRBIS indicating that they would like the UNC-Chapel Hill IRB to serve as the single IRB.
UNC Chapel-Hill IRB Responsibilities

Initial Review: When the UNC-Chapel Hill IRB has agreed to serve as the single IRB, the UNC-Chapel Hill IRB shall review and approve the protocol and initial application before Relying Institutions can be submitted for review and approval. When conducting the initial review of a single IRB study, the UNC-Chapel Hill IRB shall follow applicable policies and procedures, including submission of required materials (e.g., protocol, and as applicable, consent forms, recruitment materials, etc.).

Once the overall protocol has been approved and proposed relying parties (i.e., external institutions or individual investigators) have completed required documentation (as described in additional detail below), the UNC lead study team may submit modifications to seek UNC-Chapel Hill IRB approval of relying parties. The UNC-Chapel Hill IRB will review such relying party modifications using the expedited procedure or the convened IRB as appropriate, following procedures outlined in HRPP SOP 701. Typically, the expedited procedure will be used to review relying party modifications, so long as the relying party will conduct research in accordance with the UNC-Chapel Hill IRB-approved protocol.

Modifications to Previously Approved Research: Modifications to the overall/master protocol will be reviewed in accordance with existing UNC-Chapel Hill IRB policies/procedures. Changes to relying party/site-specific documents (e.g., consent forms, recruitment materials) must be submitted via modification and shall also be reviewed in accordance with existing UNC-Chapel Hill IRB policies/procedures.

Continuing Review: When continuing review of UNC-Chapel Hill IRB approved single IRB studies is required per regulations, the continuing review application will be reviewed in accordance with existing UNC-Chapel Hill IRB policies/procedures. The UNC lead PI is responsible for collecting and combining all information from relying parties to include in the continuing review application.

Review of Promptly Reportable Information (PRIs): The UNC-Chapel Hill IRB will review relying parties’ PRI in accordance with existing UNC-Chapel Hill IRB policies/procedures. The UNC-Chapel Hill IRB will conduct investigations and, when necessary, implement corrective actions and report determinations in accordance with the terms of the applicable reliance agreement.

Records: The UNC-Chapel Hill IRB will make available relevant IRB records, including IRB minutes and other records that document the IRB’s determinations, to the relying party upon request. When applicable, UNC-Chapel Hill IRB policy updates shall be communicated to relying parties.

3.1.6 Collaborating Individual Investigators

When a collaborating individual investigator, whether an independent investigator or an institutional investigator, is engaged in non-exempt human-subjects research, UNC-CH may choose to extend its FWA to cover the collaborating individual investigator. In such cases, an Individual Investigator Agreement outlining the terms and conditions of this arrangement must be executed by both parties.
If the investigator has a primary appointment with another institution or external organization, then UNC will request confirmation by that institution that it does not consider itself engaged by the investigator’s work on the project in order to facilitate an independent investigator agreement.