University of Tennessee College of Medicine/Erlanger Health System Institutional Review Board Reliance Agreements

To specify the procedures for executing reliance agreements between the UTCOMC and collaborating institutions.

I. SCOPE

This SOP applies to all investigators and key study personnel performing research under the auspices of the University of Tennessee College of Medicine Chattanooga IRB and its affiliated institutions.

Personnel responsible:

IRB administrative staff, IRB members, and investigators.

II. BACKGROUND

An IRB authorization agreement (or reliance agreement or cooperative agreement) is a contract between two or more organizations that delineates and documents the respective responsibilities, roles and processes of communication between an organization that provides ethical and regulatory review of human subjects research (via the reviewing IRB) and collaborating organizations that accept the determinations of the reviewing IRB (via the relying IRB(s)). Reliance agreements may cover a single study, a series of similar studies, all studies conducted by a consortium of research institutions, or all studies conducted by a relying institution. The institution providing the reviewing IRB need not be a study site (e.g., it might be a central IRB designated by a consortium of research institutions or a commercial IRB utilized by the sponsor of a multicenter study).

Under a reliance agreement, the reviewing IRB is responsible for primary IRB functions, including, but not limited to, approval of the initial study application, continuations and study revisions for all study sites subject to the agreement. The reviewing IRB or local site investigators must communicate the results of its actions and the associated documentation to the relying IRBs. The reviewing IRB must also make its policies available to the relying IRBs and provide contacts for local investigators and relying IRBs to obtain answers to questions, to express concerns, or to convey suggestions regarding its reviews. Other oversight functions are typically assigned to the relying IRBs. These latter functions include assuring the qualifications

of local investigators and their training regarding regulatory requirements, managing researcher and research staff conflicts of interest, submitting required local information for consent forms, and reporting to the reviewing IRB any unanticipated problems, protocol deviations, non-compliance by local investigators, and results of audits occurring at the local site(s). Processes for some additional oversight functions are subject to negotiation between the reviewing IRB and relying IRB in reliance agreements. These functions include clarifying local context information (e.g., special characteristics of the local subject population), reporting serious or continuing non-compliance to regulatory authorities, and completion of other required regulatory reviews related to biosafety, radiation safety, and HIPAA privacy protections, as applicable. Given the complexity of some reliance agreements, the terms of these arrangements must be reviewed in consultation with the local site investigator and fully vetted by the UTCOMC IRB before the University will enter into a reliance agreement. The initial reliance agreement must then be reviewed and approved by the UTCOMC IRB on behalf of the University. Furthermore, if another institution is requesting the addition of indemnification language to a reliance agreement, UTCOMC Sponsored Programs and/or the equivalent office at our affiliate institution(s) must review and approve this language before the University will execute the reliance agreement. At this time, the UTCOMC IRB executes reliance agreements for non-exempt human subjects research only. Exempt research for which limited IRB review takes place pursuant to §46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8) must be reviewed locally, as with other human subjects research that is exempt from HHS regulations but does not require limited IRB review.

Due to the mutual responsibilities of reviewing and relying IRBs under reliance agreements, local site investigators must maintain comprehensive communication with both the reviewing IRB and the UTCOMC IRB when UTCOMC is the relying IRB. Local investigators must register the study with the UTCOMC IRB prior to execution of the reliance agreement and later provide all communications and documents regarding actions of the reviewing IRB related to approval of the initial study application, continuations, and revisions throughout the life of the study. Changes to local key study personnel as well as information regarding unanticipated problems, protocol deviations, incidents of non-compliance, and study closure must also be communicated to the UTCOMC IRB. These communications enable the UTCOMC IRB to fulfill its monitoring responsibilities under the reliance agreement and to report its own findings to the reviewing IRB.

Recent revisions of NIH policies and Federal regulations for the protection of human subjects will significantly increase the use of reliance agreements for regulatory oversight of multicenter human research studies. The **NIH Single IRB Policy for Multi-site Research** is effective for applications with due dates on or after January 25, 2018 and contract solicitations published on or after January 25, 2018. With the exception of career development, research training and fellowship awards, this policy applies to the domestic sites of NIH-funded multi-site studies, where each site will implement the **same protocol** involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH

intramural program. For such studies, a single IRB must be designated to fulfill primary IRB functions related to approval of initial applications, continuations, and study revisions. Local sites must execute reliance agreements with the organization hosting the designated reviewing IRB in order to participate in these NIH-funded studies. Similarly, under a provision of the revised Common Rule that took effect on January 20, 2020, any institution located in the United States that is engaged in cooperative human subjects research involving multiple sites and covered by the Common Rule must rely upon approval of a single IRB for that portion of the research that is conducted in the United States. Participating sites must establish reliance agreements with the organization hosting the reviewing IRB.

In accordance with:

DHHS: 45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45 CFR 46.109(d), 45 CFR 46.114

FDA: 21 CFR 56.109(e), 21 CFR 56.114, FDA Information Sheet: Non-Local IRB Review, and Information Sheet: Cooperative Research

NIH: Policy on the Use of a Single Institutional Review Board for Multi-Site Research (June 21, 2016)

Compliance with this policy also requires compliance with state or local laws and regulations that provide additional protections for human subjects.

III. DEFINITIONS

1. **Federalwide Assurance (FWA)** is a contractual agreement between an institution engaged in human subjects research and the Office for Human Research Protections (OHRP) of the Department of Health and Human Services (HHS) in which the institution agrees to comply with federal regulations for the protection of human subjects at 45 CFR 46 in research that is conducted or supported by HHS. An institution's commitment under an FWA also applies to research conducted or supported by other federal departments and agencies that have adopted the basic federal policy for the protection of human subjects (45 CFR 46, subpart A, also known as the Common Rule) and, in that sense, it is "federalwide."

2. **IRB Authorization Agreement** (also called a **Reliance Agreement**) is a contract which documents the respective responsibilities, roles and processes of communications between an organization whose IRB provides regulatory review (i.e., the reviewing institution) and another organization that relies upon the reviewing IRB to complete primary IRB functions (i.e., the relying institution). These functions include (but are not limited to) approval of new applications, continuing reviews, and study revisions performed on behalf of the relying institution. Authorization agreements may cover a single study or multiple studies conducted by the relying institution.

3. **Non-Regulatory IRB Review** is a full board UTCOMC IRB review of a study for which it is proposed that the UTCOMC IRB serve as a relying IRB under a reliance agreement. This non-regulatory IRB review is conducted at the request of any affiliate institution for which the UTCOMC IRB serves as the IRB of record under the latter's FWA. Such a review would not count for regulatory purposes where review by a single IRB is required either by federal regulations or the funding source. Rather, the review would enable the affiliate institution to receive consultative advice regarding whether the proposed study meets general criteria and local standards for IRB approval, and whether it should be supported at the local site(s). If the study is determined to be acceptable, then official regulatory review would be provided by the IRB designated as the reviewing IRB under the reliance agreement.

4. **Overall Principal Investigator** is the individual who serves as the lead investigator for a multicenter study. The overall principal investigator will frequently be a faculty or staff member of the institution whose IRB serves as the reviewing IRB for a multicenter study. However, for arrangements like a research consortium, the designated reviewing IRB for the consortium research activities may be attached to a different institution from the institution of the overall principal investigator for a particular study.

5. **Reviewing IRB (**also called the **IRB of record)** is the IRB designated under an authorization or reliance agreement to fulfill primary IRB regulatory functions on behalf of the relying institution(s) including, but not limited to, approval of new applications, continuing reviews, and approval of study revisions. The reviewing IRB designated under a reliance agreement may be one of several types. A *central* IRB provides regulatory review for all sites participating in a consortium of institutions undertaking more than one multicenter study. The NCI CIRB is an example of a central IRB for cooperative group oncology studies. A *single* IRB is the IRB which provides regulatory review for all sites in a single, multicenter study. A single IRB will often be the IRB of the lead site for the multicenter study. An *independent* IRB is the reviewing IRB for a single multicenter study but is not associated with any of the study sites. Commercial IRBs often serve in this capacity.

6. **Relying IRB** is the IRB of an institution engaged in human subjects research that enters into an IRB authorization agreement (reliance agreement) whereby the institution cedes primary IRB review functions for research in which it is engaged to an IRB associated with another institution. Under most reliance agreements, the relying IRB continues to exercise several important responsibilities related to the regulatory oversight of the research as it is conducted at the local site(s). These include assuring the qualifications of local investigators and their training regarding regulatory requirements, managing researcher and research staff conflicts of interest, submitting required local information for consent forms, and

reporting to the reviewing IRB any unanticipated problems, protocol deviations, non-compliance by local investigators, and audit results at the local site(s).

7. **Relying Site/Institution** is an institution engaged in human subjects research that enters into an IRB authorization agreement (reliance agreement) whereby it cedes IRB review of human subjects research in which it is engaged to an IRB associated with another institution.

8. **Site Principal Investigator** is an individual who has primary responsibility for the conduct of a multicenter human subjects research study at a particular site or institution. Unless the site principal investigator is also the overall principal investigator for a multicenter study, the site principal investigator will be associated with an institution that has ceded IRB review of the study to the IRB of another institution.

IV. PROCEDURES

1. UTCOMC as the Reviewing IRB
   a. The **overall principal investigator** must first contact the **IRB Administrator** in order to determine whether the study meets the criteria for the use of an IRB Authorization Agreement (IAA) and whether the UTCOMC IRB has the capability to serve as the **reviewing IRB**. The UTCOMC IRB will also review the qualifications/expertise of the members of the UTCOMC IRB and the staff resources of the UTCOMC IRB to serve as the reviewing IRB for the study, the qualifications of the overall principal investigator to lead the study, as well as the adequacy of the research support staff to oversee the conduct of the multicenter study. The IRB Administrator, in consultation with the IRB Chair or their designee, will determine whether these criteria, as well as those below pertaining to the evaluation of proposed study sites, are satisfied.
   b. Once the UTCOMC IRB has initially agreed to serve as the reviewing IRB under a reliance agreement, the overall principal investigator must submit the study to the UTCOMC IRB via IRBNet for approval before it is initiated at any site. The submission must include all required components as follows:
      i. Application, master protocol, consent form(s), investigator's brochure(s), recruitment materials, data collection tools, etc.;
      ii. A list of **proposed relying research sites** must be included within the application, with confirmation that the external site investigator(s) have contacted their respective institution(s) to obtain any requisite local reviews and/or initiate the reliance process with their respective IRB(s);
      iii. Information regarding **local requirements** and **local research context issues** at the external site(s), which must be requested from the relying site IRB(s); and
      iv. An unsigned copy of the reliance agreement completed. (NOTE: A copy of the reliance agreement does not need to be attached to the submission if it is an **existing IRB authorization agreement** that has been fully executed and is already on file with the UTCOMC IRB. such as the overarching agreements maintained with National Cancer Institute (NCI) Central IRB (CIRB).

c. The UTCOMC IRB will evaluate the proposed relying site(s) submitted via the above- referenced IRBNet application that will address the following items:
   i. Determination of whether each relying site has a **Federalwide Assurance** and (if applicable) whether each organization uses different but equivalent protections for research not covered by HHS regulations, or whether the same policies and procedures are applied to all research conducted at the site;
   ii. Determination of whether each organization is **AAHRPP-accredited**
   iii. Evaluation of the qualifications of the site investigators and research staff, including their research workload;
   iv. Adequacy of the resources at the proposed relying site(s), including space, equipment, and personnel;
   v. Review of national, state, or local laws or regulations directly relevant to the conduct of the study at the proposed site(s);
   vi. When relevant, information about the local study population, including information about culture, race/ethnicity, socioeconomic status(es), language(s) spoken, religious affiliation(s), health literacy or general literacy level(s), and whether the local research population involves discrete and insular communities;
   vii. Information about the recruitment and informed consent processes at the local site(s), including local recruitment materials, research staff who will obtain informed consent, the location and process of the consent discussion, and primary language(s) spoken by participants and persons obtaining consent;
   viii. Information regarding whether research procedures at the local site(s) will differ from the master protocol submitted and whether sufficient resources are available at the local research site(s) to carry out the research as stated;
   ix. Determination of whether the relying organization requires any site-specific language in the approved consent document(s), such as local contacts for research participants' questions or a compensation for injury disclaimer;

x. Plans to protect the confidentiality of subjects' information, including methods of storing and transmitting paper and electronic records;
xi. If not managed centrally by a pharmacy at the organization, study-specific information about plans for the storage, handling, and dispensing of drugs and medical devices at the site(s);
xii. Determination of whether site researchers or research staff have financial or other conflicts of interest related to the research and, if so, the management plan proposed by the organization of the relying site;
xiii. Confirmation that site researchers and research staff have completed **required educational training** regarding ethical and regulatory requirements for the conduct of human subjects research;
xiv. If **required ancillary reviews** (e.g., biosafety or radiation safety reviews) must be completed at the local site, documentation regarding the outcome of those reviews; and
xv. Contact information for the organizational official or designee who will manage the reliance agreement at the relying site(s).

d. Reliance agreements will not take effect until signed on behalf of UTCOMC by the Vice Chancellor for Research as the UTCOMC institutional official's signatory designee and fully executed by the relying institution(s).
e. As the reviewing IRB, the UTCOMC IRB assumes sole responsibility for conducting review of multi-center research to determine whether it is ethically justifiable according to all applicable regulations and laws, as well as UTCOMC IRB and, if applicable, affiliate institutional policies, including the initial review of applications, continuing review, and revisions to previously approved research.
f. The UTCOMC IRB does not permit **initiation of a study** covered under the reliance agreement or the enrollment of study participants at any site until its conduct has been approved at the site by the UTCOMC IRB, the relying organization has officially confirmed its acceptance of the reliance agreement, and all other applicable requirements and approvals for the study have been secured for that site (such as biosafety and radiation safety reviews as well as requisite institutional approvals).
g. For studies subject to HHS regulations for the protection of human subjects, the UTCOMC IRB will secure, prior to initiation of research with the corresponding **vulnerable subject population** at any site, any required additional approvals from HHS when studies involve pregnant women, fetuses and neonates, children, and/or prisoners, unless an alternative process has been delineated in the reliance agreement.
h. When serving as the reviewing IRB for **studies funded by NIH**, the UTCOMC IRB acknowledges that the requirement for single IRB review applies to all awardees and participating sites in the United States but does not apply to organizations outside the United States. Participating sites may conduct their own IRB review only if it is in accord with the NIH policy on exceptions from single IRB review.
i. The UTCOMC IRB requires that researchers at all sites obtain, document, and maintain records of consent by each participant or LAR as specified in the approved study application and supporting documentation. The consent documents for each site must

also include any **locally required consent template language** as specified in the reliance agreement.

j. For the **addition of investigative sites**, the UTCOMC IRB conducts the review on an expedited basis as a minor revision to previously approved studies, using the vetting process described above.

k. When researchers or research staff at a non-federal relying institution have a **conflict of interest**, the non-federal relying institution must submit a description of the conflict of interest and proposed management plan to the UTCOMC IRB in accord with the policies of the affected site. The UTCOMC IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation in the research study and may propose additional requirements for the management plan in consultation with the non-federal relying institution. If the non-federal relying institution is unable to accept the additional elements of the management plan as negotiated, then the UTCOMC IRB cannot approve the conduct of the research at the affected site.

l. The UTCOMC IRB will ask via the questions in the reliance agreement request whether **organizational conflicts of interest** exist at participating study sites. If so, the relying institution must submit a description of the conflict of interest and proposed management plan to the UTCOMC IRB in accord with the policies of the affected site. The UTCOMC IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation of the relying site in the research study and may propose additional requirements for the management plan in consultation with the relying institution. If the relying organization is unable to accept the additional elements of the management plan as negotiated, then the UTCOMC IRB cannot approve the conduct of the research at the affected site.

m. The UTCOMC IRB has final authority for determining whether **reported events** constitute unanticipated problems involving risks to subjects or others. The UTCOMC IRB will determine whether these events require revision, suspension, or termination of the study in order to minimize the risk of harm to subjects or others. In addition, the UTCOMC IRB will report these events to institutional officials, sponsors, and federal regulatory bodies as specified in its corresponding SOP. Any additional reporting responsibilities or prerogatives of the relying organizations must be addressed in the reliance agreement.

n. The overall principal investigator must promptly provide to the UTCOMC IRB all **data and safety monitoring reports** received from the duly constituted oversight group for the study.

o. The UTCOMC IRB maintains the authority to undertake or request **audits** of the research at all participating sites, and to receive and act upon the reports of such audits, as specified in the reliance agreement.

p. The UTCOMC IRB will require participating sites to submit reports of any event involving **potential non-compliance**, including results of audits, complaints, and protocol deviations. The UTCOMC IRB will determine whether the reported event has a basis in fact, and whether it represents an instance of serious and/or continuing non- compliance, unless responsibility for this process is otherwise assigned to the relying organization(s) in the reliance agreement.

q. The UTCOMC IRB assumes final authority for determining whether identified instances of **serious and/or continuing non-compliance** require revision, suspension, or termination of the study at the affected site.

r. For studies subject to HHS and/or FDA regulations for the protection of human subjects, the UTCOMC IRB will report instances of serious and/or continuing non-compliance to institutional officials, sponsors, and federal regulatory bodies as specified in its corresponding SOP. Any additional reporting responsibilities of the relying organization(s) will be addressed in the reliance agreement.

s. The UTCOMC IRB assumes responsibility for determining the **congruency of any federal grant** supporting the research study with the activities described in the proposed study, or with the activities being undertaken in a previously approved study where the grant is obtained after initial review and approval has occurred. The UTCOMC IRB may require the lead investigator to resolve any discrepancies identified or to provide clarification regarding the reasons for apparent discrepancies.

t. Researchers and research staff at all sites must meet UTCOMC IRB requirements for training in the ethics and regulation of human subjects research, unless otherwise specified in the reliance agreement.

u. For NIH-funded studies, the UTCOMC IRB will assure that investigators meet the additional requirements of the **NIH Genomic Data Sharing Policy**, unless the process is otherwise specified in the reliance agreement.

v. The UTCOMC IRB will require that the overall principal investigator notify all site principal investigators and, if applicable, the relying organizations of all **UTCOMC IRB decisions regarding the multi-site study**, consistent with the terms of the applicable reliance agreement.

w. The UTCOMC IRB will make available relevant IRB records including, but not limited to, minutes, approved applications and protocols, approved consent forms, and other records that document the IRB's determinations, to the relying organizations upon request and as specified in the applicable reliance agreement.

x. The UTCOMC IRB will make relevant SOPs readily available to the relying organizations, including the staff of human research protections programs, and researchers and research staff, and will communicate with relying organizations via IRBNet when relevant local policies undergo major revisions that may affect any procedures covered under the reliance agreement.

y. The UTCOMC IRB will provide the name of its IRB reliance manager and contact information to the relying organizations, researchers, and research staff so that relying sites may obtain answers to questions, express concerns, and/or convey suggestions regarding the actions of the UTCOMC IRB.

z. In the event that the **reliance agreement is terminated** by either party, within 30 business days, the UTCOMC will negotiate with the relying organization to determine responsibility for oversight of any study conducted at that site and previously covered by the reliance agreement, until such time as the relevant study is closed.

aa. The UTCOMC IRB will be responsible for developing **HIPAA authorization language** in consent forms, as well as for making determinations regarding waivers or alterations of authorization under the HIPAA Privacy Rule, unless otherwise specified in the reliance

agreement. If the relying institution has required site-specific HIPAA authorization language for the consent forms or a standalone HIPAA authorization form, this language must be communicated to the UTCOMC IRB for inclusion in the site-specific consent forms or in a standalone HIPAA authorization form. Similarly, concerns of a relying institution regarding HIPAA waivers or alterations should be communicated to and negotiated with the UTCOMC IRB. Although HIPAA determinations will be made by the UTCOMC IRB unless otherwise specified in the reliance agreement, relying institutions remain solely responsible for fulfilling their obligations under the HIPAA Privacy Rule.

2. Responsibilities of Overall Principal Investigators with UTCOMC as the Reviewing IRB:
   a. The overall principal investigator and research team are responsible for understanding the requirements of the reliance agreement under which the UTCOMC IRB is serving as the reviewing IRB for the study.
   b. The overall principal investigator must work in collaboration with the UTCOMC IRB and its IRB Reliance Manager to determine and document specific roles and responsibilities for coordinating and communicating key information to relying institutions and the UTCOMC IRB as specified in the reliance agreement.
   c. The overall principal investigator must be knowledgeable about and follow all policies and procedures of the UTCOMC IRB as the reviewing IRB for the study and assure that site investigators are provided those policies and procedures.
   d. The overall principal investigator is responsible for ensuring that all relying site researchers and research staff disclose **conflicts of interest** in accord with their institutional policies. The relying institution must convey to the UTCOMC IRB any management plan that results from their local COI review process. The UTCOMC IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation of the affected personnel in the research study and may propose additional requirements for the management plan in consultation with the relying site. If the UTCOMC IRB or the relying site is unable to accept the additional elements of the management plan as negotiated, then the research cannot be conducted at the relying site. Management plans must be finalized and implemented before the study can be initiated or continued (if the conflict arises during conduct of the study) at the relying site.
   e. The overall principal investigator must ensure that relying sites do not initiate the study prior to their institutional approval of the reliance agreement and acceptance of conduct of the research study at the relying site.
   f. The overall principal investigator must also ensure that relying sites do not initiate the study covered under the reliance agreement or enroll study participants until its conduct at the relying site has been reviewed and approved by the UTCOMC IRB.
   g. The overall principal investigator must further ensure that initiation of the study or enrollment of study participants at the relying site(s) does not occur until all other applicable requirements and approvals (e.g., Institutional Biosafety Committee, Radiation Safety Committee, etc.) for the study have been secured, as specified in the reliance agreement.

h. The overall principal investigator is responsible for ensuring that information is obtained from all relying sites regarding **proposed local variations** in study conduct, recruitment materials and process, and the locally required consent language and process and communicating this information to the UTCOMC IRB.
i. The overall principal investigator is responsible for ensuring that relying sites comply with the **determinations of the UTCOMC IRB** with regard to initial review, continuing review, and review of revisions for studies covered under the reliance agreement. Communication to and acceptance of those determinations by relying sites must be documented via IRBNet by the overall principal investigator.
j. The overall principal investigator is responsible for providing relying sites and their IRBs with any **information that is requested by the relying sites**.
k. The overall principal investigator must ensure that investigators at all relying sites obtain, document, and maintain **records of informed consent** by each participant or LAR as specified by the UTCOMC IRB. The consent document(s) must also include locally required consent template language as specified in the reliance agreement.
l. The overall principal investigator is responsible for ensuring that relying study sites submit required information to the UTCOMC IRB prior to continuing review. If such information is not submitted in a timely fashion by any relying site, the overall principal investigator must report the absence of the required information in the continuing review application, inform the affected site that there is a lapse of approval at the affected site, and determine an appropriate corrective action plan in consultation with the affected site and the UTCOMC IRB.
m. The overall principal investigator must ensure that any **proposed revisions to the research at relying sites** are submitted to and approved by the UTCOMC IRB prior to implementation, except where necessary to eliminate apparent immediate hazards to the participants.
n. The overall principal investigator is responsible for promptly reporting to the UTCOMC IRB any **unanticipated problems occurring at any study site** being overseen by the UTCOMC IRB involving risks to subjects or others according to the requirements specified in the reliance agreement. These unanticipated problems must also be reported to the relying IRB after the UTCOMC IRB has made a determination.
o. The overall principal investigator must promptly provide to the UTCOMC IRB all **data and safety monitoring reports** and must provide those reports and any determinations of the UTCOMC IRB regarding revisions necessitated by the data and safety monitoring reports to relying site IRBs and investigators.
p. The overall principal investigator must cooperate with the UTCOMC IRB and the relying institutions to facilitate the completion of any **audits** conducted according to procedures specified in the reliance agreement. The UTCOMC IRB will share the results of those audits with the affected site principal investigators and institutions.
q. The overall principal investigator must promptly report to the UTCOMC IRB and relying site affected any potential instances at the study site of **non-compliance**, including results of audits, complaints, and protocol deviations. Such events initially identified at the relying sites must also be promptly reported to the UTCOMC IRB.

r. The overall principal investigator retains the obligation to provide relying sites and their IRBs with **copies of the UTCOMC IRB documents on any future actions that it takes** with respect to the study covered by the reliance agreement, such as review of revisions, continuations, protocol deviations, etc., and any suspension of subject enrollment or the study itself.
s. The overall principal investigator is responsible for ensuring that researchers and research staff at relying sites satisfy their **local requirements for training** in the ethics and regulation of human subjects research and provide documentation thereof to the UTCOMC IRB as specified in the reliance agreement.

3. UTCOMC as the Relying IRB
   a. The site principal investigator must first contact the IRB Administrator in order to determine whether the study meets the criteria for the use of an IAA and whether the UTCOMC IRB will agree to serve as a relying IRB for the multicenter study. If the study presents more than minimal risk, the UTCOMC IRB will serve as a relying IRB only if the use of a single reviewing IRB is a regulatory requirement and/or otherwise necessary for participation in the study. These circumstances include:
      i. Use of the Central IRB of the National Cancer Institute;
      ii. The funding agency or sponsor of the study requires single IRB review as a condition of funding;
      iii. Federal regulations, state laws, or local policies require the use of a single reviewing IRB; and/or

      With regard to the conduct of **minimal risk research**, the UTCOMC IRB will vet the proposed reviewing IRB according to the following considerations:
      iv. If the institution of which the reviewing IRB is a component conducts human subjects research, it has a Federalwide Assurance, provides its FWA number, and (if relevant) indicates whether the organization uses different but equivalent protections for research not covered by HHS regulations, or whether the same policies and procedures are applied to all research conducted at the site;
      v. The reliance agreement and any addenda provide assurance that the reviewing IRB will conduct its review consistent with applicable ethical standards and regulations, and will report during the study to the UTCOMC IRB any regulatory violations by or

investigations of the reviewing IRB by regulatory agencies, such as OHRP, FDA, or regulatory agencies in other countries; and/or

vi. If applicable, the UTCOMC IRB's prior experience relying on the proposed reviewing IRB.

b. For **greater than minimal risk research**, UTCOMC will permit the UTCOMC IRB to serve as the relying IRB only if the criteria set forth in (V)(3)(b)(i, ii, and/or iii) as well as the following criteria are satisfied:

i. The organization providing the reviewing IRB has an AAHRPP-accredited human research protections program or is a SMART IRB Participating Institution;

ii. The membership of the reviewing IRB is properly constituted to conduct review of the research according to applicable laws and regulations;

iii. Members of the reviewing IRB do not participate in the review of any studies under the reliance agreement with respect to which they have a conflict of interest;

iv. If applicable, the UTCOMC IRB determines that initial review of the study has been properly conducted by the reviewing IRB, based on evaluation by the UTCOMC IRB of the protocol, study application, consent forms, outcome letters and other pertinent materials submitted from the initial review of the application (e.g., questionnaires, advertisements, reviewer comments and minutes of relevant meetings when available). Further, the UTCOMC IRB may request that the reviewing IRB re-evaluate its determination in light of any concerns identified by the UTCOMC IRB in its administrative review of the submission;

v. If applicable, the UTCOMC IRB determines that the results of any HHS or FDA audits of the reviewing IRB conducted within the last five years are satisfactory; and

vi. Brief review of the SOPs of the reviewing IRB determines that they satisfy all applicable federal regulatory requirements.

c. During this time, the site principal investigator will be advised to wait for confirmation that UTCOMC is amenable to relying on the proposed reviewing IRB prior to registering the study in IRBNet or submitting the study to the proposed reviewing IRB.

d. If the study does not meet the initial criteria for reliance on an external IRB, the site principal investigator will be advised to submit an IRBNet application for local IRB review.

e. When **vetting the reviewing IRB**, the UTCOMC IRB will assess the qualifications of the designated external IRB to serve as the reviewing IRB. The IRB Administrator, in consultation with the IRB Chair or their designee, will determine whether these criteria are satisfied. If the reviewing IRB does not meet UTCOMC's requisite qualifications, the site principal investigator will be advised to submit an IRBNet application for local IRB review.

f. If UTCOMC determines the designated external IRB possesses the requisite qualifications to serve as the reviewing IRB, the site principal investigator will be provided with documents delineating UTCOMC's local requirements, the **UTCOMC Boilerplate Consent Form Language document**, and advised to incorporate all applicable local requirements into the lead study team's initial submission for the reviewing IRB or the modification request for the addition of UTCOMC as a site if the initial submission has already been approved by the reviewing IRB. The study, or the

modification for the addition of UTCOMC as a site, should not be submitted to the reviewing IRB until the study has been registered in IRBNet and the UTCOMC IRB has acknowledged, via an outcome letter in IRBNet, that local requirements have been fully satisfied.

g. The site principal investigator must **register the study with the UTCOMC IRB** via IRBNet, and receive a final acknowledgement letter, before the study is initiated at this site. The IRBNet application will collect basic study information and ask questions to assess for requisite local ancillary reviews and other procedures (e.g., execution of data use agreements, etc.). The application must include all required components as follows:
   i. Documents that will be submitted to the reviewing IRB, such as the application, protocol, consent form(s), investigator's brochure, package inserts, recruitment materials, data collection tools, etc., with UTCOMC's local requirements having been incorporated according to (V)(3)(g);
   ii. If the main study has already received approval from the reviewing IRB, a copy of the most recent IRB approval letter(s) (i.e., initial and continuing) that contain the current approval and expiration dates for the overall study as well as the regulatory categories and/or level of review under which the main study was approved; and
   iii. An unsigned copy of the proposed reliance agreement completed (NOTE: A copy of the reliance agreement does not need to be attached to the submission if the study will be conducted under an existing IRB authorization agreement that has been fully executed and is already on file with the UTCOMC IRB, such as the overarching agreements maintained the National Cancer Institute (NCI) Central IRB (CIRB), , etc.).

h. Upon receipt of the IRBNet application, the UTCOMC IRB will review the following elements of the submission:
   i. The qualifications of the site principal investigator and site investigator(s), and the adequacy of the research support staff, to serve as a local site for a multicenter study;
   ii. The documents submitted to ensure UTCOMC's local requirements have been properly incorporated; and
   iii. The terms set forth in the reliance agreement, which may warrant further review by the UTCOMC Office of Sponsored Programs as described below in (V)(3)(l).

i. Once the IRBNet application has been reviewed and the UTCOMC IRB has determined that all local documentation requirements have been satisfied, an outcome letter will be issued via IRBNet to the site principal investigator, study contact(s), and institutional contacts as applicable. The outcome letter will grant **permission for the acknowledged study materials to be submitted to the reviewing IRB** and will also include an administrative recommendation to send the final, approved documents and fully executed reliance agreement to the UTCOMC IRB in IRBNet as soon as they become available. At this time, the reliance agreement will be signed by the UTCOMC Institutional Official and sent to the reviewing IRB for full execution. Upon receipt of the final, IRB-approved study documents and fully executed reliance agreement, the UTCOMC IRB will review the documentation for accuracy.
   i. If the documentation is accurate and appropriate, a final acknowledgment letter will

be sent to the site principal investigator.

ii. If the documentation contains errors, such as the reviewing IRB's modification of required boilerplate language, administrative recommendations will be issued for corrections and a final acknowledgment letter will be issued upon receipt of the IRB-approved, corrected study documentation.

j. If an institution of which the reviewing or a relying IRB is a component requests the inclusion of **specific liability and/or indemnification language** in the reliance agreement, then the UTCOMC Office of Sponsored Programs must review and approve the language before the University will enter into a reliance agreement incorporating the proposed language.

k. The reviewing IRB will be responsible for developing **HIPAA authorization language** in consent forms, as well as for making determinations regarding waivers or alterations of authorization under the HIPAA Privacy Rule, unless otherwise specified in the reliance agreement. If the UTCOMC IRB has site-specific language that is required as part of the HIPAA authorization in its consent forms, this language will be communicated to the reviewing IRB for inclusion in the site-specific consent forms. Similarly, concerns of the UTCOMC IRB regarding HIPAA waivers or alterations will be communicated to and negotiated with the reviewing IRB. Although HIPAA determinations will be made by the reviewing IRB unless otherwise specified in the reliance agreement, UTCOMC remains solely responsible for fulfilling its obligations under the HIPAA Privacy Rule.

l. The study may not be initiated at the local site(s) prior to UTCOMC and local site **institutional approval** of the reliance agreement and acceptance of the research application by the UTCOMC IRB and any engaged affiliate institution via a final acknowledgement letter sent from IRBNet. Further, the UTCOMC IRB does not permit local initiation of a study covered under the reliance agreement or the local enrollment of study participants until its conduct at the local site(s) has been reviewed and approved by the reviewing IRB, and until all other applicable requirements and approvals (e.g., Institutional Biosafety Committee, Radiation Safety Committee, etc.) for the study have been secured.

m. Reliance agreements will not take effect until signed on behalf of UTCOMC by the Vice Chancellor for Research as the UTCOMC institutional official's signatory designee and fully executed by the reviewing institution.

n. When the UTCOMC IRB will serve as a relying IRB for more than one study under the same applicable reliance agreement (such as when relying on the CIRB or participating in a research consortium), the vetting process described above will occur only at the time of the initial reliance agreement request when the same reviewing IRB will be used for subsequent studies, unless UTCOMC specifies otherwise.

o. The UTCOMC IRB retains the prerogative to conduct a **non-regulatory, full board review** of any study for which it may serve as the relying IRB under a reliance agreement, if a request is made for such review by an affiliate institution for which it serves as the IRB of record under the latter's FWA.

p. The UTCOMC IRB will comply with the **determinations of the reviewing IRB** regarding initial review, continuing review, review of revisions, reportable events, as well as DSMB and device reports for studies covered under the reliance agreement. Documentation of these determinations must be provided within 10 business days of the reviewing IRB's determination by the site principal investigator to the UTCOMC IRB via the **Documents from Reviewing IRB** submission form in IRBNet.

q. The UTCOMC IRB will instruct local researchers, and their research staff, that they must cooperate with the reviewing IRB in its execution of responsibilities for initial review, continuing review, review of revisions, reportable events, as well as DSMB and device reports for the studies covered by the reliance agreement, that they must adhere to the **reviewing IRB's policies and procedures**, and that they must provide information requested by the reviewing IRB in a timely manner.

r. The UTCOMC IRB will provide to the reviewing IRB or site principal investigator any requested information regarding **local requirements and local research context issues** prior to the reviewing IRB's review of the conduct of the study at the local site(s).

s. For studies subject to HHS regulations for the protection of human subjects, the UTCOMC IRB will be responsible for seeking required **additional approvals from HHS** when studies at the local site(s) involve pregnant women, fetuses and neonates, children, or prisoners, unless an alternative process has been delineated in the reliance agreement.

t. The UTCOMC IRB requires that researchers obtain, document, and maintain records of consent, assent, and parental permission by each participant, LAR, and parent/legal guardian as specified by the reviewing IRB. The consent, assent, and parental permission documents must also include **locally required consent template language** as specified in the reliance agreement.

u. The UTCOMC IRB requires that any **proposed revisions in research** must be submitted beforehand to the reviewing IRB and cannot be implemented without prior approval by the reviewing IRB, except where necessary to eliminate apparent immediate hazards to the participants.

v. The UTCOMC IRB requires its researchers and research staff to disclose **conflicts of interest (COIs)** in accord with UTCOMC and UTCOMC IRB policies. The UTCOMC IRB will convey to the reviewing IRB any management plan that results from the local COI review process. The reviewing IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation of the affected personnel in the research study and may propose additional requirements for the

management plan in consultation with the UTCOMC IRB. In the event that the reviewing IRB considers additional elements appropriate for the management plan, the UTCOMC IRB will negotiate the terms of a final plan. If UTCOMC or the reviewing IRB is unable to accept the additional elements of the management plan as negotiated, then the research cannot be conducted at the local site(s). Management plans must be finalized and implemented before the study can be initiated or continued (if the conflict arises during conduct of the study) at the local site(s).

w. The UTCOMC IRB will determine whether an **organizational conflict of interest** exists at the local study site. If so, the UTCOMC IRB will submit a description of the organizational conflict of interest and proposed management plan to the reviewing IRB. The reviewing IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation of the relying site in the research study and may propose additional requirements for the management plan in consultation with UTCOMC. If UTCOMC or the reviewing IRB is unable to accept the additional elements of the management plan as negotiated, then the research cannot be conducted at the local site(s).

x. The UTCOMC IRB requires that researchers promptly report to the reviewing IRB any **local unanticipated problems** involving risks to subjects or others according to the requirements specified in the reliance agreement. These unanticipated problems must also be reported to the UTCOMC IRB no less than 10 business days after the reviewing IRB has made a determination via form in IRBNet.

aa. Local investigators must promptly provide to the UTCOMC IRB all **data and safety monitoring reports** as well as **device reports** received from the overall principal investigator or the reviewing IRB no less than 10 business days after the reviewing IRB has made a determination via forms in IRBNet.

bb. The UTCOMC IRB can **audit** studies in cooperation with the reviewing IRB and according to any procedures specified in the reliance agreement. The results of those audits will be shared with the site principal investigator and the reviewing IRB by the UTCOMC IRB.

cc. The site principal investigator must promptly report to the reviewing IRB and the UTCOMC IRB any potential instances of **non-compliance**, including results of audits, complaints, and protocol deviations. Such events initially identified by the UTCOMC IRB will be promptly reported to the reviewing IRB by the UTCOMC IRB.

dd. The UTCOMC IRB will determine whether incidences of **serious or continuing non-compliance** require suspension or termination of such studies at the local site(s), unless an alternative process has been delineated in the reliance agreement.

ee. For studies subject to HHS and/or FDA regulations for the protection of human subjects, the UTCOMC IRB will determine whether any incident of non-compliance is serious or continuing and requires reporting to institutional officials and sponsors, including the federal government, unless an alternative process has been delineated in the reliance agreement.

ff. Researchers and research staff at the local site(s) must meet UTCOMC IRB requirements for **training in the ethics and regulation of human subjects research**, unless otherwise specified in the reliance agreement.

gg. For NIH-funded studies, the UTCOMC IRB will assure that local investigators meet the additional requirements of the **NIH Genomic Data Sharing Policy**, unless responsibility for this process is otherwise specified in the reliance agreement.

hh. The UTCOMC IRB will promptly notify the reviewing IRB when **local policies undergo major revisions** that may affect the determinations assigned to the reviewing IRB under the reliance agreement, such as policies affecting reliance agreements or local context considerations.

ii. The UTCOMC IRB will provide the site principal investigator and research staff with information regarding the local IRB Administrator from whom they may obtain answers to questions, express concerns, and/or convey suggestions regarding the use of the reviewing IRB.

jj. In the event that the **reliance agreement is terminated** by either party, within 30 business days, the UTCOMC IRB will assume responsibility of oversight for any study conducted at the local site(s) and previously covered by the reliance agreement, until such time as the relevant study is closed or a reliance agreement is established with another institution.

4. Responsibilities of Site Principal Investigators with UTCOMC as the Relying IRB
   a. The site principal investigator and research team are responsible for understanding the **requirements of the reliance agreement** under which the local site is participating in the study.
   b. The site principal investigator must be knowledgeable about and follow **the reviewing IRB's policies and procedures** as outlined in its SOPs and ensure that other site investigators and research staff are provided those policies and procedures.
   c. The site principal investigator may not **initiate the study** covered under the reliance agreement or enroll study participants until its conduct at the local site(s) has been approved by the reviewing IRB.
   d. The site principal investigator may not initiate the study at the local site(s) prior to UTCOMC and local site institutional approval of the reliance agreement and acceptance of the research application by the UTCOMC IRB via a final acknowledgement letter sent from IRBNet.
   e. The UTCOMC IRB does not permit local initiation of a study covered under the reliance agreement or the local enrollment of study participants until all other applicable requirements and approvals (e.g., Institutional Biosafety Committee, Radiation Safety Committee, full execution of applicable data use agreement(s) and/or material transfer agreement(s), etc.) for the study have been secured.
   f. The site principal investigator must comply with the **determinations of the reviewing IRB** with regard to initial review, continuing review, review of revisions, reportable events, as well as DSMB and device reports for studies covered under the reliance agreement. Documentation of these determinations must be provided within 10 business days of the reviewing IRB's determination by the site principal investigator to the UTCOMC IRB via the **Documents from Reviewing IRB** submission form in IRBNet.
   g. The site principal investigator must provide information requested by the reviewing IRB (e.g., differences in local procedures and/or resources, reports pertaining to the

conduct of the research at the local site(s), investigator qualifications, etc.) in a timely manner.

h. The site principal investigator must obtain, document, and maintain records of consent, assent, and parental permission by each participant, LAR, and parent/guardian as specified by the reviewing IRB. The consent, assent, and parental permission documents must also include **locally required consent template language** as specified in the reliance agreement.

i. The site principal investigator is responsible for submitting any **proposed local revisions in the research** to the reviewing IRB, which cannot be implemented without prior approval by the reviewing IRB, except where necessary to eliminate apparent immediate hazards to the participants.

j. The site principal investigator is responsible for ensuring that all local researchers and research staff disclose **conflicts of interest** in accord with UTCOMC and UTCOMC IRB policies. The UTCOMC IRB will convey to the reviewing IRB any management plan that results from the local COI review process. The reviewing IRB assumes final authority for determining whether the proposed management plan is sufficient to allow participation of the affected personnel in the research study and may propose additional requirements for the management plan in consultation with the UTCOMC IRB. In the event that the reviewing IRB considers additional elements appropriate for the management plan, the UTCOMC IRB will negotiate the terms of a final plan. If UTCOMC or the reviewing IRB is unable to accept the additional elements of the management plan as negotiated, then the research cannot be conducted at the local site(s). Management plans must be finalized and implemented before the study can be initiated or continued (if the conflict arises during conduct of the study) at the local site(s).

k. The site principal investigator is responsible for promptly reporting to the reviewing IRB any **local unanticipated problems** involving risks to subjects or others according to the requirements specified in the reliance agreement. These unanticipated problems must also be reported to the UTCOMC IRB after the reviewing IRB has made a determination.

l. The site principal investigator must promptly provide to the UTCOMC IRB all **data and safety monitoring reports** as well as **device reports** received from the overall principal investigator or reviewing IRB no less than 10 business days after the reviewing IRB has made a determination about the data and safety monitoring reports and device reports.

m. The site principal investigator must cooperate with the reviewing IRB and the UTCOMC IRB in the completion of any **audits** conducted according to procedures specified in the reliance agreement. The results of those audits will be shared with the site principal investigator by the UTCOMC IRB.

n. The site principal investigator must promptly report to the reviewing IRB and the UTCOMC IRB any potential instances at the local site(s) of **non-compliance**, including results of audits, complaints, and protocol deviations. Such events initially identified by the UTCOMC IRB will be promptly reported to the reviewing IRB.

o. The site principal investigator is responsible for ensuring that local researchers and research staff meet UTCOMC IRB requirements for **training** in the ethics and regulation

of human subjects research, unless otherwise specified in the reliance agreement.

p. The site principal investigator is responsible for submitting all **changes to local key study personnel**, including the addition or removal of local personnel, replacement of the site principal investigator, as well as modification of study roles, via the forms in IRBNet prior to implementation of the changes. The UTCOMC IRB will issue an acknowledgement letter from IRBNet documenting acceptance of the changes, at which time the requested changes may be implemented.