1.0 Purpose:

1.1 This policy defines the requirements and procedures that the Hartford HealthCare Human Research Protection Program (HHC HRPP) and the Institutional Review Board (IRB) follow for review of human subjects research when requested by the principal investigator (PI) to allow reliance on an external IRB or independent (commercial) IRB or when review by a single IRB is required for NIH-supported multi-site studies conducting research at more than one domestic site.

1.2 The HHC Signatory Official or his/her designee has the ultimate authority regarding whether or not to rely on an external or independent IRB.

1.3 The HHC IRB may rely on the IRB of another institution or organization for review and approval of human research if such reliance benefits HHC, its patients, and its investigators.

1.4 An independent (commercial) IRB may be used by employed medical staff and medical staff with privileges at HHC who are otherwise not employees.

1.5 To qualify for external IRB oversight, an active reliance agreement must exist between Hartford HealthCare and the external IRB's institution. When HHC relies on an Independent IRB for review and approval of human research, the relationship is documented with an IRB Authorization Agreement (IAA). External IRBs should be accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), except when this is not possible.

2.0 Definitions:

2.1 **Authorization Agreement**, which is also called a reliance agreement, is the agreement that documents respective authorities, roles, responsibilities, and communication between an institution/organization providing the ethical review and a participating site relying on the sIRB.

2.2 **Independent (commercial) IRB** is not affiliated with an academic institution

2.3 **Multi-site study** uses the same protocol to conduct non-exempt human subjects research at more than one site.

2.4 **Participating site** in a multi-site study is a domestic entity that will rely on the sIRB to carry out the site's IRB review of human subjects research for the multi-site study.

2.5 **sIRB** (single IRB)is the selected IRB of record that conducts the ethical review for participating sites of the multi-site study.

3.0 Research Ineligible for Use of an Independent (commercial) IRB

3.1 Investigator-initiated trials (non-federally funded or supported)
3.2 Studies in which an HHC investigator is the IND holder
3.3 Studies involving Vulnerable Populations
3.4 Studies with significant local community impact
3.5 Studies involving high risk surgical intervention

4.0 Research Qualifying for Review by an External or Independent (commercial) IRB

4.1 HHC will apply the following criteria when considering to allow the use of an External or Independent IRB:

4.1.1 Clinical trials where HHC is participating as a Memorial Sloan-Kettering Cancer Center Clinical Trials Site pursuant to the executed Cooperative Research Agreement.

4.1.2 NCI Cooperative Group trials utilizing the National Cancer Institute (NCI) Central Institutional Review Board (CIRB)

4.1.3 A NIH-funded/supported multi-site study mandating use of a single IRB located in the U.S.

4.1.4 Outpatient, multi-center clinical trials of investigational drugs (Phase II, III, or IV) regardless of sponsor

4.1.5 Instances in which an Institutional Conflict of Interest (COI) in research may affect - or reasonably appear to affect – institutional processes for the design, conduct, reporting, review, or oversight of research.

4.2 HHC will also consider investigator experience and qualifications when deciding whether to allow the use of an External or Independent IRB.

5.0 NIH single IRB Requirements

5.1 NIH expects that all domestic sites participating in multi-site studies, which involve non-exempt human subjects research funded wholly or in part by the NIH, including grants, cooperative agreements, and Research and Development (R&D) contracts will use a single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects.

5.2 Exceptions to this policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception.

5.2.1 On November 22, 2019, as permitted by 45 CFR 46.114(b)(2)(ii), the Office for Human Research Protections (OHRP) announced in the Federal Register its determination of exception for two categories of research from the required use of a single IRB to review cooperative research under the Revised Common Rule. Relevant OHRP exception categories for NIH-supported cooperative research include the following circumstances:

5.2.1.1 the NIH single IRB policy does not apply, and the research was initially approved by an IRB before January 20, 2020

5.2.1.2 NIH excepted the research from its single IRB policy before January 20, 2020

5.2.1.2.1 the following NIH-funded multi-site studies being conducted at more than one domestic site may continue to use multiple IRBs for the duration of the exception granted by NIH to the NIH sIRB policy, and no later than the next competing award (i.e. new and/or revision).

5.2.1.2.1.1 Studies for which NIH approved an exception from its single IRB policy before January 20, 2020

5.2.1.2.1.2 Studies conducted under ongoing, non-competing awards with receipt dates prior to January 25, 2018 if an IRB initially approved the research prior to January 20, 2020

5.3 As of January 20, 2020, studies subject to the Revised Common Rule Cooperative Research Provision (45 CFR 46.114(b)) must use a single IRB as required by the terms and conditions of award. This includes studies that are not subject to the NIH sIRB policy – such as domestic, multisite career development (K) and fellowship (F) awards.

5.4 Grant applicants are expected to include a plan for the use of a sIRB in the grant applications and contract proposals submitted to the NIH.

5.4.1 The sIRB plan should include the following elements:

5.4.1.1 Describe how you will comply with the NIH Policy on the Use of sIRB for Multi-Site Research.
5.4.1.2 If available, provide the name of the IRB that is anticipated to serve as the sIRB of record.
5.4.1.3 Indicate that all identified participating sites will agree to rely on the proposed sIRB and that any sites added after award will rely on the sIRB.
5.4.1.4 Briefly describe how communication between sites and the sIRB will be handled.
5.4.1.5 Indicate that all participating sites will, prior to initiating the study, sign an authorization/reliance agreement that will clarify the roles and responsibilities of the sIRB and participating sites.
5.4.1.6 Indicate which institution or entity will maintain records of the authorization/reliance agreements and of the communication plan.

5.5 At this time, when an HHC Investigator is the awardee of a multi-site grant, the HHC IRB intends to serve as the sIRB for awards that include less than 5 additional participating sites. Multi-site awards including more than 5 participating sites will be considered on a case-by-case basis.

6.0 Procedure:

6.1 Prior Consultation

6.1.1 To avoid duplication of effort and frustration, it is highly suggested that investigators and study teams consult with the HRPP office prior to engagement with an Independent IRB if there is any question as to whether the HHC IRB may accept that IRB's review of a specific research protocol.

6.1.2 The investigator and study team should collaborate with the HRPP office to ensure addition of local-context language into the informed consent template prior to submission to the reviewing IRB.

6.2 To ensure that HHC maintains a record of all research conducted by our organization, regardless of whether the research is overseen by our local IRB or an external IRB, the PI must submit the study into the electronic submission system through a Research Application. By submitting an application, the study will proceed through our usual workflow, thereby receiving the applicable ancillary reviews and approvals.

6.3 The PI must indicate in the HHC Research Application that s/he requests a deferred review in the "*Institutional Affiliations/Local Collaboration*" and "*Outside IRB*" sections of the application when an external IRB will responsible for oversight of the study.

6.4 For initial review of the application, the PI must provide the HHC IRB with a copy of:

6.4.1 The letter of approval from the external reviewing IRB;

6.4.2 The final approved protocol and informed consent;

6.4.3 The entire grant, if applicable, exclusive of appendices;

6.4.4 Any other documents considered by the IRB in making its determination to approve the study, including relevant Investigator's Brochure(s), package insert(s), advertisements, surveys, questionnaires, phone scripts, and other participant materials.

6.5 The HHC IRB Chair/Vice Chair or the HRPP Director will perform a facilitated review of the research protocol and the external IRB's decisions and determinations to ensure that:

6.5.1 The HHC investigators and staff conducting the research are appropriately qualified;

6.5.2 The study meets HHC Research Institute standards;

6.5.3 Other applicable institutional approvals, such as, Radiation Safety have been obtained before research begins;

6.5.4 Those actions and determinations made by the reviewing IRB meet HHC standards for initial review, continuing IRB review or review of modifications to previously approved research;

6.5.5 No concerns about local research context are present;

6.5.6 The consent form complies with HHC standards and requirements, including applicable HHC standard template local context language

6.6 Possible Review Determinations

6.6.1 HHC retains the authority to accept the reviewing IRB's approval, or to make minor changes through the HHC facilitated review process, or to require review by a convened HHC IRB.

6.6.2 The HHC IRB Chair/Vice Chair or HRPP Director will either:

6.6.2.1 Accept the reviewing IRB approval;

6.6.2.2 Accept the reviewing IRB approval with minor modifications;

6.6.2.3 Not accept the reviewing IRB approval and refer the study to a convened HHC IRB for review.

6.7 If the reviewing IRB approval is accepted, the investigator and external IRB office will be sent written notification by the HHC IRB that the reviewing IRB is designated as the **IRB of Record**.

6.7.1 The PI is responsible for providing the IRB of Record with all required study materials for initial and continuing review, adverse event reporting, study modifications, non-compliance and unanticipated problems, in accordance with HHRP policies and procedures.

6.8 The HHC HRPP must receive copies of all:

6.8.1 Correspondence relating to the study including initial and continuing approval letters from the reviewing IRB;

6.8.2 Progress reports;

6.8.3 Modifications to the study and applicable approval letters and documents;

6.8.4 Reports of serious or continuing non-compliance, unanticipated problems and suspensions or termination of approval.

6.9 Adverse events are to be reported to the IRB of Record in accordance with that IRB's policy. If a HHC adverse event appears to rise to the level of an Unanticipated Problem requiring prompt reporting, the PI must also report the event to the HHC IRB.

6.10 The HHC PI is responsible for establishing communication procedures to ensure the HHC HRPP receives all IRB documentation for studies deferred to an external IRB.

6.11 The HHC HRPP will process all correspondence in accordance with the procedures outlined in the active reliance agreement or IAA.

6.12 Studies deferred under this policy continue to be subject to all other HHC research administrative requirements, including Radiation Safety review, CITI Training in human subjects protection, disclosure and management of Financial Conflicts of Interest, HRPP and Grants and Contracts monitoring and audit procedures, and budget and Clinical Trial Agreement/contract review.

6.13 All HRPP policies and procedures apply to studies deferred under this policy.

7.0 Division of Responsibilities

7.1 The division of responsibilities between the reviewing IRB and the relying IRB will be outlined through a written reliance agreement.

7.1.1 The written reliance agreement must define the responsibilities of the relying organization and reviewing IRB, including but not limited to:

7.1.1.1 Determining which organization is responsible for obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, and neonates; or children; or prisoners.

7.1.1.2 A description of the process to ensure IRB approval is obtained when the organization is responsible for a multi-site research study outside the United States that is not required to follow requirements for single IRB review.

7.1.1.3 A description of the process used by the awardee organization to ensure authorization agreements are in place, and that documentation is maintained.

7.1.1.4 A description of which organization is responsible for meeting additional certification requirements, such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.

7.1.1.5 A description of the process to document the rationale for not relying upon a single IRB review in accordance with NIH policy on exceptions from single IRB review.

7.2 The **reviewing IRB** ("IRB of Record"):

7.2.1 Ensures the structure and composition of the IRB is appropriate to the research reviewed and complies with applicable laws. This includes ensuring the IRB is properly constituted; members are appropriately qualified; that members do not participate in the review of studies in which they have a conflict of interest; and the IRB follows policy to separate business functions from ethics review services.

7.2.2 Conducts review of research to determine that research is ethically justifiable, according to all applicable regulations and laws, including initial review, continuing review, and review of modifications to previously approved research.

7.2.3 Conducts review of the addition of investigative sites to previously approved protocols. The IRB may decide to review these additions as separate protocols or as modifications to previously approved research, and they may decide to handle such modifications using the expedited procedure rather than the convened IRB for review. When the expedited procedure is used, the IRB must specify the criteria for when the addition of an investigative site is considered to be a minor modification.

7.2.4 Ensures the IRB has the final authority to decide whether researcher or research staff conflict of interest and its management, if any, allows the research to be approved.

7.2.5 Reviews unanticipated problems involving risks to participants or others.

7.2.6 Has the authority to suspend or terminate IRB approval.

7.2.7 Notifies the researcher, and if applicable the organization, of its decisions, consistent with any reliance agreement.

7.2.8 Makes available relevant IRB records, including but not limited to minutes, approved protocols, consent documents, and other records that document the IRB's determinations to the relying organization upon request.

7.2.9 Has authority to request an audit of research being reviewed.

7.2.10 Makes relevant IRB policies readily available to the relying organization, including HRPP staff, and researchers and research staff, and having a mechanism for communicating to the organization when policies are updated, as appropriate.

7.2.11 Specifies the contact person and provides contact information for the reviewing IRB for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the IRB.

7.3 The **relying IRB** and its investigators and research staff:

7.3.1 Are knowledgeable about the need to obtain any approvals from HHC prior to seeking review by another IRB, and that researchers know when to seek guidance.

7.3.2 Ensure that researchers and research staff have appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes and guidance governing their research, and are knowledgeable about the organization's policies and procedures.

7.3.3 Comply with the determinations and requirements of the reviewing IRB.

7.3.4 Provide the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB's determination, prior to IRB review.

7.3.5 Notify the reviewing IRB when local policies that impact IRB review are updated.

7.3.6 Ensure that officials of the relying organization may not approve the research subject to the reliance agreement if it has not been approved by the reviewing IRB.

7.3.7 Acknowledge that researchers must cooperate in the reviewing IRB's responsibility for initial and continuing review, record keeping, and reporting, and that all information requested by the reviewing IRB must be provided in a timely manner.

7.3.8 Requires researchers and research staff to disclose conflicts of interest according to the process agreed upon between HHC and reviewing IRB, and comply with any conflict of interest management plans that may result

7.3.9 Reports promptly to the reviewing IRB any proposed changes to the research. The investigator cannot implement changes to the research

(including changes in the consent document) without prior review and approval, except where necessary to eliminate apparent immediate hazards tithe participants.

7.3.10 Will not enroll participants in research prior to review and approval by the reviewing IRB, and meeting all other applicable requirements and approvals for the study.

7.3.11 When responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative.

7.3.12 Reports promptly to the reviewing IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement.

7.3.13 Provides to the reviewing IRB data safety monitoring reports they receive, according to the IRB's reporting policy.

7.3.14 Reports non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement.

7.3.15 Conducts monitoring in addition to, or in cooperation with, the reviewing IRB, when appropriate.

8.0 Reliance Upon an IRB that is not AAHRPP-accredited

8.1 In the absence of accreditation, HHC must take steps, based on the risks posed by the research, to ensure participants in the research are adequately protected.

8.2 For minimal risk research HHC may:

8.2.1 Obtain an assurance from the non-accredited IRB that it will conduct its review consistent with the applicable ethical standards and regulations, and that it will report any regulatory violations or investigations of the reviewing IRB by regulatory agencies, such as OHRP, the FDA, or regulatory agencies in other countries.

8.2.2 Request the reviewing IRB to attest that it has completed its own internal quality review process.

8.3 For more than minimal risk research, HHC may:

8.3.1 Request to review meeting minutes or other IRB records related to the research

8.3.2 Evaluate the reviewing IRB's policies/procedures

8.3.3 Conduct audits of the IRB

9.0 Documentation:

9.1 Research Administration will maintain all records related to the implementation of this policy, electronic communications and notifications to investigators, funding or regulatory agencies, etc.

9.2 HRPP records will be archived for a period of at least three years following the termination or completion of the research activities.

10.0 References:

10.1 45 CFR 46 Subpart A – *Basic HHS Policy for Protection of Human Research Subjects* [45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45 CFR 46.109(d), 45 CFR 46.114)

10.2 Guidance on Engagement of Institutions in Human Subjects Research, October 16, 2008

10.3 HRPP Policy #600: *Engagement in Research*

10.4 Terms of Assurances for FWA: http://www.hhs.gov/ohrp/assurances/assurances/filasurt.html

10.5 Sample template for a Reliance Agreement also known as an Institutional Review Board Authorization Agreement (IAA): http://www.hhs.gov/ohrp/assurances/forms/irbauthorizpdf.pdf

10.6 Hartford HealthCare Federalwide Assurance #00021932

10.7 NOT-OD-16-094 Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (June 20, 2016)

10.8 NOT-OD-18-004 Guidance on Implementation of the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (October 11, 2017)

10.9 NOT-OD-18-003 Guidance on Exceptions to the NIH Single IRB Policy (October 11, 2017)

10.10 NOT-OD-20-058 Additional Guidance on the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (January 22, 2020)

11.0 Attachments:

11.1 List of organizations with established HHC reliance agreements and independent IRBs

12.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
01	EHP	7/1/11	New Issue
02	CLB	3/24/15	Updated section of research application to request use of external IRB; Updated FWA # for HHC; Update list of institutions in which HHC has a Cooperative Review Arrangement or IAA.
03	CLB	4/15/16	Added Sections 3.0 and 4.0 to detail the specific situations in which an external IRB may or may not be

			utilized. Added minor clarifications throughout.
04	CLB	1/2/18	Revised Sections 4.0
05	CLB	3/15/20	Updated policy to meet AAHRPP Standard I-9. Added information relevant to NIH Policy on Use of sIRB for Multi-Site Research
06	CLB	8/5/20	Expanded Section 7.1 to detail additional requirements to be included in the written reliance agreement

Standard I-2, Standard I-9, Element II.2.I.

ATTACHMENT:

Institutions with Reliance Agreements and Independent IRBs that may be relied upon:

A. Hartford HealthCare Reliance Agreements

1. Connecticut Children's Medical Center
2. University of Connecticut Health Center
3. University of Connecticut, Storrs
4. The Jackson Laboratory
5. Memorial Sloan-Kettering Cancer Center
6. National Cancer Institute Central IRB
7. Participating Institution - SMART IRB (Streamlined, Multisite, Accelerated Resources for Trials IRB Reliance)

B. AAHRPP Accredited Independent IRBs

1. Western Institutional Review Board, Inc. (WIRB)
2. Copernicus Group IRB
3. ADVARRA
4. Sterling IRB
5. IntegReview
6. BRANY (Biomedical Research Alliance of New York)

For a complete listing of accredited IRBs, visit, https://www.aahrpp.org/learn/find-an-accredited-organization