1.0 Purpose:

1.1 The purpose of this policy is to describe the responsibilities of and procedures followed by the Hartford HealthCare Human Research Protection Program (HHC HRPP) and Institutional Review Board to ensure that research conducted at HHC is designed in such a way that risks to subject are minimized while meeting high standards of scientific integrity.

2.0 Definitions:

2.1 **Investigator** – the principal investigator and any other person who is responsible for the design, conduct, or reporting of research

3.0 Procedure:

3.1 The HHC IRB uses a combination of methods to ensure a complete review of each proposed protocol's scientific or scholarly validity. During initial and continuing review of research protocols, the IRB collaborates with other institutional and non-institutional review committees, and, when needed, independent consultants to assess the scientific or scholarly validity of a proposed research study.

3.2 **Investigator Responsibilities and Requirements in Designing Ethical Research**

3.2.1 Federal regulations outlined in 45 CFR 46.111 and 21 CFR 56.111 require that:

3.2.1.1 Investigators use sound scientific design in the conduct of research.

3.2.1.2 Investigators and research staff monitor participants for potential harm and take steps to minimize or mitigate those harms when possible.

3.2.1.3 Investigators and research staff follow policies and procedures for reporting so that the IRB and other entities within the organization can monitor the rights and welfare of participants enrolled in research.

3.2.2 Protocols should be designed so that the research will develop or contribute to generalizable knowledge. When investigators do not design the study, they should judge the design to be sound enough to meet its objective before agreeing to enroll patients.

3.2.3 As part of their obligation to protect participants, investigators should understand the concept of minimizing risk, and should consider study designs that minimize risks. A description of the rationale used for choosing the procedures and a risk to potential benefit analysis should be included in research protocols.

3.2.4 Investigators must ensure that the resources necessary to protect participants are present before conducting the research study, including:

3.2.4.1 Sufficient time to conduct and complete the research.

3.2.4.2 A process to ensure that all participants assisting with the research are adequately informed about the protocol and their research-related duties and functions.

3.2.4.3 Access to a population that will allow recruitment of the necessary number of participants.

3.2.5 A research protocol document written by the investigator(s) and submitted to the Hartford HealthCare Research Institute for eventual IRB review must include the eleven (11) areas discussed below:

3.2.5.1 Literature Review - includes relevant background, a discussion of the differences from currently published research, and the areas of specific importance that the research will provide.

3.2.5.2 Specific Aims/Hypotheses – describes the purpose of the study, the area being evaluated, and the specific aims (both primary and secondary); for clinical trials and other explanatory research, hypotheses need to be clearly stated; for descriptive or exploratory studies, research questions appropriately substitute for hypotheses.

3.2.5.3 Clinical Significance - - describes the study's clinical significance and its relationship to improving clinical care.

3.2.5.4 Research Design - includes the structure of the experiment, whether it is retrospective, prospective, or randomized, and how many samples or study participants will be involved.

3.2.5.5 Sampling/Enrollment Criteria - discusses the inclusion and exclusion criteria; for example demographics, medical or other contraindications, and the rationale for such choices. For retrospective studies, the period of sampling should be defined.

3.2.5.6 Methods of Data Collection - provides study timeline and procedures, describes method of data collection (e.g., chart review, patient interview, etc.), variables and outcomes to be collected and how each will be measured, provides rationale and contents for any new measures, prescribes a sample size determination/power calculation (often part of statistics section).

3.2.5.7 Use of Specimens – describe any specimen tissue collection procedures; if the study involves the use of previously banked tissue, identify the source.

3.2.5.8 Statistical Analysis Plan –this sections describes the statistical test(s) to be used, explains how these will be applied to the data, should also include alpha level and other parameters (e.g., sidedness, ITT, PP), sample size needed based on power analysis (if not done above), provides information on the software to be used for such analysis.

3.2.5.9 Data security, Storage and Privacy – this sections should describe where data will be stored, what protection(s) safeguard(s) the data, how data will be exchanged/transmitted (e.g., HHC Outlook e-mail, encrypted flash drive), and what steps will be used to minimize use and sharing of PHI

3.2.5.10 The Benefit/Significance to HHC and its Patients - includes a discussion of the significance to the hospital mission and its patients; describes clinical benefit / utility.

3.2.5.11 References - unless the research is on an absolutely new area – there should be sufficient literature to include a minimum of 3 prior studies; may be in any standard format (AMA, APA)..

3.3 **Pre-IRB Scientific Review Procedures**

3.3.1 Research projects requesting internal funds available through the Research Endowment Fund (i.e. small grant, new investigator, open competition) or Medical Staff Fund will first be reviewed and considered by the Scientific Review Committee (SRC) for scientific validity and merit.

3.3.1.1 This Committee may include members of the Board of Directors, Administration, Medical and other staff at Hartford HealthCare and is chaired by the Vice President for Research. Members have advanced degrees (M.D. and PhD) in various disciplines and in most cases are experienced researchers themselves.

3.3.1.2 The Committee meets once per month.

3.3.1.3 Protocols are reviewed based on criteria related to methodology, feasibility, and significance.

3.3.1.4 Final communications to investigators from the SRC (when funding is awarded) make it clear that the need for IRB review will be considered by the HRPP and, if required, will proceed.

3.3.1.5 The HRPP is copied on funding decision letters. These are then included in the packet of material for IRB review.

3.3.2 Scientific integrity of Unfunded and Externally Funded research projects will be reviewed prospectively by the Research Institute Departmental Scientific Review Group and any issues identified during that review will be resolved prior to review by the IRB.

3.3.2.1 This review group is composed of four (4) Senior Scientists with advanced degrees (PhD) in various disciplines. Each Senior Scientist covers the particular clinical areas in which they have expertise most closely related to their field of study.

3.3.2.2 The reviewer considers the criteria outlined on the "*Checklist for Scientific Review of Research Proposal*". This criteria mirrors the elements of a research protocol that are described above in section 3.2.5.

3.3.2.2.1 Protocols that have already undergone peer-review by an external federal funding agency, such as the National Institutes of Health, will be accepted as such and will not be given further scientific review.

3.3.2.3 Incoming protocols are assigned and reviewed by a single Senior Scientist. If the reviewer identifies significant issues with a protocol, however, the group will convene a meeting in which they systematically address and discuss the potential flaws and determine the course required to reach a resolution.

3.3.2.4 Documentation of this review and disposition will be provided to the IRB along with the standard study materials.

3.4 IRB Assessment of Study Design

3.4.1 Only those studies deemed to be scientifically sound, as determined by the procedures describe above will be reviewed by the Institutional Review Board (IRB).

3.4.2 To approve research activities, the HHC IRB shall determine that the protocol satisfies all of the following requirements:

3.4.2.1 Risks to subjects are minimized by using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and

3.4.2.2 Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

3.4.2.3 Risks to subjects are reasonable in relation to the anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result.

3.4.3 In order for the IRB to make these determinations, they will take into consideration information provided in the following documents, which will be made available to all reviewers:

3.4.3.1 A completed Research Application, which includes sections that allow investigators to describe where and by whom participants will be recruited, languages spoken of the study population, collection, use, and storage of data, At a minimum, this must include the signed application forms, including information regarding sponsor and support services needed to conduct the research,

3.4.3.2 The full protocol developed by the investigator or sponsor protocol for multi-center clinical trials, and the Public Health Service (PHS) or other applicable funding agency grant application

3.4.3.3 Investigator's brochure, if applicable, or a summary of any pre-clinical data and pertinent clinical data

3.4.3.4 "Checklist for Scientific Review of Research Proposal" or Scientific Review Committee approval letter

3.4.3.5 Informed Consent Form

3.4.3.6 Any planned recruitment advertisements.

3.4.4 The primary reviewer, an IRB member who presents the protocol to the convened board, reviews the comments of the HHC Research Institute Departmental Scientific Review Group or the determination of the Scientific Review Committee and any other pre-IRB-submission reviewers to ensure that prior recommendations either were addressed by the investigator or are noted as requiring further consideration by the board. While the board's review does not require the level of disciplinary expertise necessary for merit or peer review by a funding agency, IRB members are oriented to perform a thorough and detailed review of the study and, if possible, to discuss and resolve any unanswered questions with the investigator before presentation to the convened board.

3.4.4.1 All members are oriented in the use of the "IRB Reviewer Checklist for New Protocols" and the "IRB Reviewer Checklist for Continuation (Progress Reports)" which prompt reviewers to consider whether each of the criteria for IRB approval of research has been met (45 CFR 46.111 and 21 CFR 56.111).

3.4.5 In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies received if the subject did not participate in the research). The IRB will not consider possible long range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those risks that fall within the purview of its responsibility.

3.4.6 When reviewing clinical trials subject to ICH-GCP(E6), the IRB will take into consideration available non-clinical and clinical information about the investigational product being studied to ensure its adequacy to support the proposed clinical trial. This is done by a review of the Clinical Investigator's Brochure (commonly referred to as the CIB or IB). The primary reviewer assigned to the protocol will be responsible for evaluating the available information.

3.4.7 The Use of Consultants

3.4.7.1 A consultant, who is not a member (regular, alternate, or ad hoc) of the IRB, may be requested to provide professional or expert advice in a particular area when the IRB needs added scientific or scholarly expertise. The consultant should be independent of the investigator and protocol. He or she must receive all relevant information available to the IRB in order to perform an in-depth review of the research, and must understand the background, aims and methods of the research. The consultant is asked to attend the IRB meeting to present his/her findings relative to the scientific validity of the study and risks and benefits to subjects, and to answer questions; however, if the consultant is unavailable to attend the meeting, s/he may provide written comments for distribution to the IRB members in attendance.

3.4.7.2 HRPP Policy #610 – "*Use of Consultants/Ad Hoc Members in IRB Review*" describes in more detail the process to determine that a consultant is needed, the process to obtain a consultant,

and the ways in which information provided by a consultant is communicated and documented.

4.0 Documentation:

4.1 The HHC HRPP office will maintain all protocol documentation and minutes of IRB meetings and any pre-IRB review scientific validity evaluations.

4.2 Records will be archived for a period of at least six (6) years following the termination or completion of the research activities.

5.0 References:

5.1 45 CFR 46.111(a)(1)(i), 45 CFR 46.111(a)(2)

5.2 21 CFR 56.111(a)(1)(i), 21 CFR 56.111(a)(2)

5.3 ICH GCP: 2.4, 2.5

5.4 Institutional Review Board Management and Function, Bankert, E. A., Amdur, R. J., 2nd Edition, 2006

6.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
00	EHP	7/1/11	New issue
01	CLB	11/18/14	Updated section 3.2.5; added “Use of Specimens” and “Clinical Significance”
02	CLB	7/22/15	Added minor clarification in section 3.4.6 to address ICH-GCP
03	CLB	3/15/20	General review and minor corrections.

Elements I.1.F. and II.1.E.