1.0 Purpose:

1.1 Under institutional authority and federal regulations [45 CFR 46.108(a)(4), 45 CFR 46.113, 21 CFR 56.108, 21 CFR 56.113], Institutional Review Boards (IRB) are responsible to oversee the safety of research participants and may suspend or terminate human research that:

1.1.1 Is not being conducted in accordance with the federal, state and institutional requirements, or

1.1.2 Has been associated with unexpected serious harm to participants.

1.2 The Hartford HealthCare Institutional Review Board (HHC IRB) may approve human subjects research that meets the criteria set forth in government regulations, organizational policies, and other federal and state laws and regulations. Approval notices to the Principal Investigator (PI) detail any special conditions or requirements for conduct of the research and provide a time limit on the approval period.

1.3 The PI is responsible for conducting the approved research in accordance with the IRB requirements, as well as with all ethical standards, organizational policies, federal or state laws or regulations applicable to the research study.

1.4 The purpose of this policy is to identify instances of non-compliance that must be reported to the IRB by investigators and describe how they are handled by the IRB.

2.0 Definitions:

2.1 **HRPP** – Human Research Protections Program

2.2 **OHRP** – Office for Human Research Protections

2.3 **Non-compliance:** Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with either the research plan as approved by the IRB, or federal regulations or institutional policies governing such research.

2.4 **Allegation of Non-compliance:** an unproven assertion of non-compliance.

2.5 **Serious non-compliance:** Any behavior, action or omission in the conduct or oversight of human research that has been determined to:

2.5.1 Affect the rights and welfare of participants and others;

2.5.2 Increase risks to participants and others, decreases potential benefits or otherwise unfavorably alters the risk/benefit ratio;

2.5.3 Compromise the integrity or validity of the research; or

2.5.4 Result from the willful or knowing misconduct on the part of the investigator(s) or study staff.

Examples include, but are not limited to: Conducting non-exempt research that requires direct interaction or interventions with human subjects without first

obtaining IRB approval; enrolling subjects who fail to meet the inclusion or exclusion criteria in a protocol that involves greater than minimal risk and that, in the opinion of the IRB Chair, designee or convened IRB, places the participants at greater risk; or failure to report adverse events, unanticipated problems, or substantive changes to the proposed protocol without seeking approval from the IRB.

2.6 **Continuing Non-compliance:** A pattern of non-compliance that if allowed to continue is likely to increase risk to subjects, adversely affect the rights, welfare and safety of research subjects, or adversely affect the scientific integrity of the study.

2.7 **Non-serious and Non-continuing Non-compliance:** any behavior, action or omission in the conduct or oversight of research involving human subjects that deviates from the approved research plan, federal regulations or institutional policies but, because of its nature, research project or subject population, does not:

2.7.1 Place, or have the potential to place, participants and others at greater risk than previously anticipated;

2.7.2 Have a substantive effect on the value of the data collected; and

2.7.3 Result from willful or knowing misconduct on the part of the investigator(s) or study staff.

Examples include, but are not limited to: Changing study personnel without notifying the IRB; shortening the duration between planned study visits; implementing minor wording changes in the study questionnaires without first obtaining IRB approval.

3.0 Procedure:

3.1 The actions of anyone conducting, reviewing or approving research may result in non-compliance. Examples of non-compliance include:

- Performing human subjects' research without obtaining IRB approval or a declaration of exemption.
- Deviating from or violating the provisions of an IRB approved protocol.
- Failing to secure IRB approval of a protocol due for periodic continuing review prior to its expiration date.
- Permitting a protocol's IRB approval to lapse without stopping all research-related activities and submitting a Progress or Closure Report to the IRB.
- Failure of the IRB to document in its meeting minutes or supporting documents, protocol-specific findings supporting the IRB's determinations for waiver or alteration of the consent process, approval of research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children.
- Failure of the Research Institute to determine concordance between the industry contract and the proposed consent document regarding payment for study participation and payment in the event of a research-related injury.

3.2 Information regarding non-compliance may come to the attention of the IRB from a number of different sources, including new applications, research summaries and progress reports from investigators, internal audits, FDA audit reports, monitoring activities by sponsors, adverse event/safety reports, members of the research team, participants or their family members, community members, and other sources. Each confidential complaint or concern is taken seriously and reviewed in a consistent, prompt, and professional manner.

3.3 It is the obligation of the PI and study team to submit a written report to the IRB within 7 calendar days of any occurrence of non-compliance that is suspected to be serious or continuing. Reports must contain enough information to determine whether the report is sufficiently credible so that potential evidence of non-compliance may be identified and acted upon.

3.4 **Initial Assessment of Reports of Non-compliance**

3.4.1 All reports of non-compliance (i.e., allegations of non-compliance and all self-reported non-compliance) will be initially reviewed by the HRPP Director.

3.4.2 Within five (5) business days of receipt, the HRPP Director or designee will evaluate the report or allegation and determine the nature of the non-compliance.

3.4.3 Based on a preliminary review of available information, communication with the principal investigator(s) involved in alleged non-compliance activities, and the seriousness of the allegations, the Director, in collaboration with the IRB Chair, will determine if immediate suspension of study procedures and/or study enrollment is required for the project in question, as well as for other projects under the same investigator.

3.4.4 If suspension is required, the principal investigator(s) involved in the allegations and associated research staff personnel, Department Head(s), and Institutional Official (IO) are notified in writing. Federal regulatory agencies are notified, if applicable, and, in the case of externally funded studies, notice is sent to the sponsor.

3.4.5 Otherwise, non-compliance that is neither serious nor continuing will follow the process under “Handling Non-compliance that is neither serious nor continuing” described below.

3.4.6 Non-compliance that is serious or continuing will follow the process under “Handling Non-compliance that is serious or continuing”.

3.4.7 The HRPP Director may continue with the investigation, assign the investigation to HRPP staff, or refer to an investigative group assigned by the IRB.

3.5 **Handling Non-compliance that is neither serious nor continuing**

3.5.1 An investigation of the non-compliance may involve examination of study records, as well as discussion with the complainant (if not anonymous), principal investigator, research team, research participants and/or family members, witnesses and others as appropriate.

3.5.2 Upon completion of the investigation, the HRPP Director, along with the IRB Chair, determines whether any corrective actions are needed, and communicates this to the involved individuals.

3.5.3 The Director or designee will work with the individuals to implement the corrective action plan and ensure that all requirements are completed.

3.5.4 If the involved individuals do not implement the corrective action plan, the matter will be considered to be continuing non-compliance and the procedures in that category will be followed.

3.6 **Handling Non-compliance that is serious or continuing**

3.6.1 The HRPP Director or investigative group will prepare a complete written report documenting the serious or continuing non-compliance, the findings of the investigation, the current status of the protocol (suspended, or not), and any recommended corrective actions.

3.6.2 This report will be sent to the IO and the non-compliance referred to a convened IRB for review and action. A special meeting may be called, if necessary.

3.6.3 The IRB members will receive copies of all investigative documents, the original IRB application, as well as, the currently approved protocol and consent documents. All members are expected to review the documents prior to the meeting.

3.6.4 The assigned investigator(s) will attend the meeting and provide a summary of the information gathered during the investigation.

3.6.5 The Principal Investigator may be invited to attend the meeting and allowed an opportunity to respond to the allegation(s).

3.6.6 The IRB may meet with the complainant (if not anonymous) and others as needed.

3.7 **Actions of the convened IRB**

3.7.1 The convened IRB will confirm by vote whether they feel the non-compliance is serious or continuing.

3.7.2 If the IRB determines the non-compliance is not serious or continuing, the matter will be referred back to the HRPP Director along with any recommendations. The Director will determine the corrective actions that are needed, communicate this to those involved and will ensure that the corrective actions are completed.

3.7.3 If the IRB confirms the non-compliance is serious or continuing, it will consider the following actions:

- Suspension of the research. (This may be done immediately if necessary to eliminate apparent immediate hazards to the research subjects.)
- Termination of the research.
- Notification of current participants (required when such information might relate to participants' willingness to continue to take part in the research.
- Modification of the protocol.
- Modification of the information disclosed during the consent process.
- Additional information must be provided to past participants.
- Requirement that current participants re-consent to participation.
- Modification of the continuing review schedule.

- Monitoring of the research.
- Monitoring of the consent.
- Obtaining more information pending a final decision.
- Referral to other organizational entities such as legal counsel, risk management, institutional official (IO).
- Provide additional recommendations to the IO.
- Other actions appropriate for the non-compliance.

3.8 **Final Authority**

3.8.1 The IO has the final authority to confirm the IRB's recommendation of serious and/or continuing non-compliance..

3.8.2 The IO may authorize additional investigation utilizing members drawn from appropriate divisions in the Hartford Healthcare to further consider the non-compliance. Findings will be reported to the IO within a reasonable time frame as described by the IO.

3.9 **Reporting**

3.9.1 The IO or designee will report the institution's determinations and findings to all appropriate entities within Hartford HealthCare, and to relevant regulatory agencies as described in HRPP Policy #930 – "*Reporting to Institutional Officials and Regulatory Agencies*".

3.9.2 All correspondence will be filed in the applicable study file.

4.0 Documentation:

4.1 The HHC HRPP office will maintain all records related to the implementation of this policy, electronic communications, and notifications to investigators, funding or regulatory agencies, etc.

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 46.108(a)(4)(i), 45 CFR 46.116c)(5)

5.2 21 CFR 50.25(b)(5), 21 CFR 56.108(b)(2), 21 CFR 56.113

5.3 Reporting Incidents to OHRP: Guidance on When and How to File Incident Reports (June 20, 2011)

6.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
00	EHP	7/1/11	New issue
01	CLB	3/15/20	General review; update regulatory citations

Elements **I.5.D.** and II.2.H..