1.0 Purpose:

1.1 Consistent with federal regulations, the Hartford HealthCare Human Research Protection Program (HHC HRPP) has the authority to suspend or terminate approval of research that is not being conducted in accordance with the requirements or determinations of the Institutional Review Board (IRB) or that has been associated with unexpected serious harm to subjects. Suspensions may be directed by the convened IRB, IRB Chair, HRPP Director or designee. Additionally, the Institutional Official (IO) may suspend or terminate research approved by the IRB for human subject protection, administrative, and financial reasons.

1.2 This policy establishes compliance with the regulatory requirement in 45 CFR 46.108(a)(4)(ii) and 21 CFR 56.108(b)(3) that IRBs have written procedures ensuring prompt reporting of any suspension or termination of an approved protocol to the IRB, institutional official (IO), Office for Human Research Protections (OHRP), and, when applicable, the Food and Drug Administration (FDA).

2.0 Definitions:

2.1 **Administrative Hold:** A voluntary action by a Principal Investigator (PI) or sponsor to temporarily or permanently stop some or all approved research activities in response to a finding or concern that <u>does not</u> adversely affect the safety, rights and welfare of research subjects. In this case, an administrative hold is not considered a suspension or termination.

2.2 **Expiration (Lapse) of IRB Approval:** If a PI has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the expiration date specified by the IRB, such a research study has expired (lapsed).

2.3 **Study Closure:** A process by which any study that has active IRB approval is completed and/or stopped voluntarily by the PI. This includes studies that never enrolled subjects or in which the research has been completed and there is no longer a need to access to identifiable data. This process is most often initiated by the PI, but can be initiated by actions of other involved parties, including study sponsors or the IRB.

2.4 **Suspension:** An action by the convened IRB, IRB Chair, the HRPP Director or a designee to stop, temporarily or permanently, some or all previously approved research activities short of permanently stopping all research activities. Suspended protocols are not closed with the IRB and require continuing review by the IRB.

2.5 **Termination:** An action by the convened IRB to permanently stop all activities of a previously approved research protocol. Terminated protocols are closed protocols, and they no longer require continuing review.

3.0 Procedure:

3.1 **Administrative Holds**

3.1.1 The PI or the sponsor may place a research study on administrative hold and must notify the IRB in writing of this action. This may be done in instances where an interim data analysis is being conducted to determine if enough events have occurred to meet the determined level of statistical significance, for example.

3.1.2 Written notification from the PI to the IRB must include the following information:

- The intent to voluntarily place a study on administrative hold in response to a request to do so.
- A description of the research activities that will be stopped.
- The proposed actions to be taken to protect current subjects or a statement that the administrative hold is not believed to adversely affect the safety, rights and welfare of research subjects.
- The actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm to research subjects.

3.1.3 Upon receipt of the written notification from the PI, HRPP Director, in consultation with the IRB Chair if necessary, determines whether any additional procedures are needed to protect the rights and welfare of current research subjects.

3.1.4 Many times an administrative hold will be followed by a protocol amendment; the PI should submit an "IRB Request for Modification/Amendment" as appropriate.

3.2 Suspensions/Terminations by Investigators, Sponsors, or other Regulatory Authorities

3.2.1 Suspensions or termination imposed by a PI, sponsor, or regulatory body, such as the FDA, because it is in the best interest of the subjects (following findings by a Data Safety and Monitoring Board, for example) must be communicated to the IRB of the decision within seven (7) calendar days of the PI deciding to or learning of the suspension or termination.

3.2.2 The PI must provide the IRB with the reasons why the study is being suspended or terminated. If only some of the study activities will be suspended (such as suspension of enrollment) then the PI must include a description of what activities will continue and why it is appropriate to do so.

3.2.3 The IRB will review the notification and determine if additional protection of research subjects, corrective actions, or investigation is required. The IRB will notify the principal investigator in writing of whether or not the IRB concurs or if additional actions are required.

3.3 Immediate Suspension or Termination of IRB Approval by the IRB Chair, HRPP Director or IO

3.3.1 The Chair, HRPP Director or IO considers whether any actions are needed to protect the rights and welfare of current subjects, and orders

any actions that need to be taken to eliminate an apparent immediate hazard prior to review by the convened IRB. This may include:

- Withdrawing subjects from the study that are currently on active treatment;
- Determining if subjects will be placed at risk of harm by withdrawing them from the study; and
- Allowing subjects to continue to be monitored for safety reasons.

3.3.2 The HRPP Director documents the reason(s) for the suspension and the required actions that are to take place.

3.3.3 The suspension or termination and associated actions are communicated to the PI in writing.

3.3.4 The suspension or termination is placed on the agenda of the next convened IRB meeting.

3.3.5 All IRB members receive a copy of the current protocol, consent documents and any supporting information relevant to the suspension or termination.

3.3.6 The person who ordered the suspension or termination attends the meeting or provides a written report if unable to attend.

3.3.7 The convened IRB votes to continue, modify, or lift the suspension or termination.

3.3.8 If the IRB votes to continue or modify the suspension or termination, then:

- The IRB considers whether any action is needed to protect the rights and welfare of current subjects and votes on the actions to be taken.
- The IRB documents in the IRB minutes the reason for the suspension, and if applicable, any actions ordered to take place.
- The IRB considers whether any additional procedures are needed to protect the rights and welfare of current subjects.
- The IRB Chair or designee communicates these findings to the PI in writing.

3.4 **Protection of Currently Enrolled Subjects**

3.4.1 Before a suspension is put into effect, the convened IRB, or if time does not permit, an IRB Chair, HRPP Director or designee, considers whether any additional procedures are needed to protect the rights and welfare of current subjects.

3.4.1.1 Such procedures might include:

- Transferring subjects to another PI.
- Making arrangements for clinical care outside of the research.
- Allowing continuation of some research activities under the supervision of an independent monitor.
- Notification of current subjects.
- Notification of former subjects.

3.4.2 For terminated studies, the convened IRB, or if time does not permit, an IRB Chair, HRPP Director or designee, considers whether any additional procedures are needed to protect the rights and welfare of current subjects, such as:

- Requiring or permitting follow-up of subjects for safety reasons.
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor.

3.5 **Examples of Reasons for Suspension/Termination**

3.5.1 The IRB, IRB Chair, the HRPP Director or IO may immediately suspend the conduct of research for a variety of reasons. These include but are not limited to the following types of circumstances:

- PI fails to provide additional information requested by the IRB at a time during the current approval period that the IRB feels is necessary for it to conduct continuous oversight of the study.
- New information becomes available that could alter the original determination by the IRB to approve the study.
- Reports of unanticipated problems occurring at a greater frequency than previously expected.
- The PI fails or appears to fail to comply with federal regulations or HRPP policy regarding the protection of human subjects (non-compliance).
- The PI fails to meet the stipulations imposed by the IRB at continuing review within the time frame allotted by the IRB.
- Falsification of study data.

3.6 **Study Closure and Expiration (Lapse) of IRB Approval**

3.6.1 **Study Closure Initiated by the PI**

3.6.1.1 Studies that are completed, meaning there is no need for continued use of identifiable private information for research purposes, such as data analysis or transmission, preparation of a study publication, or internal or external audit, may be closed by the PI.

3.6.1.2 The PI must submit the “IRB Closure Report” Form, a summary of findings and results (preferably in manuscript form), and a comprehensive list of publications resulting from the research.

3.6.1.3 The HRPP Director or designee documents the study completion and forwards the information to the Institutional Official (IO) for review and acknowledgement of study closure.

3.6.1.4 The closure is reported at the next convened IRB via the agenda.

3.6.2 **Administrative Suspension and Closure Due to Expiration (Lapse) of IRB Approval**

3.6.2.1 The expiration date for an IRB protocol is the first date that the protocol is no longer approved. Investigators are notified as described in *HRPP Policy #628 – "Continuing Review Notification"* when a protocol is nearing its expiration date and what the requirements are for requesting continuation of a protocol. If the IRB has not approved the protocol by the expiration date cited on the most recent "Notice of Progress Report Due" sent to the investigator, IRB approval expires automatically and the study is considered suspended, denoted as "Lapse of Approval – Expired" in the IRB electronic system.

3.6.2.2 All research activity, including recruitment and enrollment of new subjects, advertisement, screening, interventions and/or interactions with existing subjects, the collection of identifiable private information from existing subjects, and the analysis of existing identifiable private information, must stop.

3.6.2.3 If no written reply is received from the PI to the "Suspension Notice" issued by the HRPP Director within 60 days, the study is then administratively closed. It may only be re-opened by submission of a new Research Application to the IRB.

3.6.2.4 The convened IRB is notified of administrative closures via the agenda.

3.6.2.5 This expiration (lapse) of IRB approval is not reported to OHRP or FDA as a suspension or termination of IRB approval under DHHS or FDA regulation.

3.6.2.6 **However, it is important to note that a lapse of IRB approval or administrative closure for failure to submit the required information needed by the IRB to provide continued oversight of human subjects research constitutes <u>non-compliance</u>. As such, if a particular investigator or study team is in the habit of submitting required reports late such that suspension or termination of research occurs, this will be considered continuous non-compliance and subject to reporting to institutional authorities and federal agencies, as applicable.** (*See HRPP Policy #925 – "Handling of Non-compliance and Policy #936 – "Reporting to Institutional Officials and Regulatory Agencies")*

3.7 **Reporting Requirements**

3.7.1 The IO or designee, with assistance from the HRPP Director, report the institution's determination 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"

3.7.2 All correspondence is filed in the individual 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)(ii), 45 CFR 46.113

5.2 21 CFR 56.108(b)(3), 21 CFR 56.113

5.3 ICH-GCP: 4.12.3

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

5.5 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)
01	EHP	7/1/11	Conversion to new policy template; significant expansion of policy
02	CLB	3/15/20	

Elements: I.5.D., II.2.G., **II.2.H**., III.2.D.