1.0 Purpose:

1.1 Investigators are responsible for conducting human subjects research in accordance with all applicable federal and state regulations, Hartford HealthCare Human Research Protections Program (HHC HRPP) policies and procedures, and the specific requirements of the Institutional Review Board (IRB) that reviewed the research study. Changes to the IRB-approved protocol, planned or otherwise, are governed by federal regulations and HRPP policies and procedures.

1.2 All exceptions to approved protocols need approval from the IRB and any applicable sponsor or regulatory agency (i.e., FDA) prior to implementation. If prior approval is not requested, implementation would constitute a **protocol violation.**

1.3 This policy does not apply to emergency protocol deviations where changes to a study are made without prior IRB approval to eliminate apparent immediate hazards to participants.

2.0 Definitions:

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

2.2 **Protocol Exception -** A one time, intentional action or process that departs from the IRB-approved study protocol, intended for one occurrence or applied to a single individual. This action is approved by the sponsor or funding agency, IRB, and the FDA, if applicable, prior to its implementation. An example of an exception may include: the potential enrollment, following approval of the sponsor, of a participant who fails to meet all of the protocol eligibility criteria.

Note: Any permanent change to a protocol constitutes an amendment that must be submitted to the IRB for approval prior to initiation.

2.3 **Protocol Violation:** Any protocol deviation or exception that may affect the subject's rights, safety, or well being and/or the completeness, accuracy and reliability of the study data.

The following are examples of protocol violations:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent(s) or informed consent obtained after initiation of study.
- Informed consent for IND/IDE studies obtained by someone other than individuals authorized by IRB to obtain consent, e.g. someone other than a licensed physician investigator.
- PI prescribing or administering the wrong drug on the study
- Performing study procedure not approved by the IRB.
- PI failure to report a serious adverse event to the IRB and/or sponsor.

3.0 Procedure:

3.1 **Investigator Responsibilities**:

3.1.1 Submit the "*Request for Protocol Exception*" Form to the IRB with sufficient justification for how the protocol exception serves the best interest of the participant.

3.1.2 Supporting documentation of pre-approval of the protocol exception by the sponsor and/or FDA, if applicable, must be included.

3.1.3 Maintain all documentation of pre-approval by the sponsor and/or FDA, if applicable, and IRB approval of the exception in the research study file.

3.2 **IRB Responsibilities**:

3.2.1 Protocol exceptions may be reviewed either by the expedited review process or by the convened board depending upon the type of research and nature of the exception request.

3.2.2 If the research involves an investigational agent (drug, biologic, or device) prior approval of the protocol exception by the sponsor and/or funding agency is also required.

3.2.3 When the research involves an investigational significant risk device and the protocol exception may affect the scientific soundness of the plan or the rights, safety, or welfare of the participants, FDA pre-approval is also required [21 CFR 812.150(4)].

3.2.4 The IRB Chair or designee will determine the level of review required for the protocol exception.

3.2.5 Expedited review may be conducted by the IRB Chair or by one or more of the experienced IRB members designated by the Chair.

3.2.5.1 For expedited review, the assigned reviewer(s) receive:

3.2.5.1.1 The current approved protocol;
3.2.5.1.2 The "*Request for Protocol Exception*" Form;
3.2.5.1.3 Protocol Summary Abstract;
3.2.5.1.4 Current IRB-approved consent form.
3.2.5.1.5 Supporting documents and other pertinent materials.

3.2.5.2 The protocol exception is evaluated to determine if the exception will increase the risk to the participant or jeopardize the integrity of the research data.

3.2.5.3 The reviewer(s) may:

3.2.5.3.1 Approve the exception as written;
3.2.5.3.2 Require modifications; or
3.2.5.3.3 Refer to the full committee for review.

3.2.5.4 If expedited review, at the next convened meeting, all IRB members are informed via the agenda of any items that have been approved under this procedure

3.2.6 Full Board review

3.2.6.1 If the protocol exception is to be reviewed by the convened IRB, all board members will receive:

3.2.6.1.1 The Protocol Exception Form;
3.2.6.1.2 Protocol Summary Abstract;
3.2.6.1.3 Current IRB-approved consent form; and
3.2.6.1.4 Supporting documents.

3.2.6.2 The primary reviewer will receive the above materials plus:

3.2.6.2.1 The current approved protocol; and
3.2.6.2.2 Any additional pertinent material.

3.2.6.3 Possible decisions that can be made by the board include:

3.2.6.3.1 Approve the exception as submitted;
3.2.6.3.2 Require modifications;
3.2.6.3.3 Table the exception until further justification or information is received; or
3.2.6.3.4 Disapprove.

3.2.6.4 The IRB meeting minutes document the discussion of the convened board review and final determination.

3.2.7 The investigator is notified in writing detailing the final determination of the IRB.

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)(3)(iii) – *Assuring compliance with this policy-research conducted or supported by any Federal Department or Agency*

5.2 21 CFR 56.108(a)(3) and (4)- *IRB functions and operations*

5.3 21 CFR 312.66 – *Assurance of IRB Review*

5.4 21 CFR 812.150 (a)(4)– *Investigational Device Exemptions - Reports*

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