1.0 Purpose:

1.1 The purpose of this policy is to define the procedures the Hartford HealthCare Human Research Protections Program (HHC HRPP) follows when reporting: (1) any unanticipated problem involving risks to subjects or others; (2) any serious or continuing non-compliance with Department of Health and Human Services (DHHS) or Food and Drug Administration (FDA) regulations or the requirements or determinations of the Institutional Review Board (IRB); or (3) any suspension or termination of IRB-approved human subjects research.

1.2 The policies and procedures for prompt reporting and IRB review of reports of unanticipated problems, non-compliance, and suspensions or terminations of IRB-approved human subjects research are covered in separate IRB policies, which include *Unanticipated Problems/Adverse Event Reporting*, *Handling of Non-compliance*, and *Suspension or Termination of Research.*

1.3 Non-exempt human subjects research and clinical investigations that require IRB review are subject to this policy.

2.0 Definitions:

2.1 **Human subjects research** - activities that meet the DHHS definition of *research* and involves a *human subject* as defined by DHHS or meets the FDA definition of *clinical investigation* and involves a *human subject* or *subject* as defined by FDA. The DHHS definition for *research* and *human subject* and the FDA definition for *clinical investigation*, *human subject*, and *subject* are provided below:

2.2 **Research** - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(l)]

2.3 **Human subject** - a living individual about whom an investigator (whether professional or student) conducting research (1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens or (2) Obtains, uses, studies, analyzes, or generates Identifiable private information or identifiable biospecimens..

2.4 **Intervention** - physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

2.5 **Interaction** – communication or interpersonal contact between investigator and subject.

2.6 **Private information** - information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)(1)(2)]

2.7 **Clinical investigation** - any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding non-clinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous. [21 CFR 50.3(c) and 21 CFR 56.102(c)]

2.8 **Human subject** - an individual who is or becomes a participant in research, either as a recipient of the *test article* or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

2.9 **Test article** - any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

2.10 **Subject** - a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or have a medical condition or disease [21 CFR 812.3(p)].

3.0 Procedure:

3.1 Consistent with federal regulations, the HHC HRPP is responsible for reporting on behalf of the institution:

3.1.1 any unanticipated problems involving risks to subjects or others;

3.1.2 any serious or continuing non-compliance with DHHS or FDA regulations or the requirements or determinations of the IRB; or

3.1.3 any suspension or termination of IRB-approved non-exempt human subjects research to the applicable institutional officials and, as required or appropriate, to the applicable regulatory agencies.

3.2 The Federalwide Assurance (FWA) of Hartford HealthCare applies to federally supported or conducted human subjects research. In general, the same criteria and process for the conduct and oversight of human subjects research, for determinations about reportable events, and for actions taken in response to such events will apply to all human-subjects research in which Hartford HealthCare is engaged, regardless of funding source.

3.2.1 If such an event involves human subjects research that is <u>not</u> federally conducted or supported, the IRB is not required to report the event to the Office for Human Research Protections (OHRP) or other relevant federal department or agency head (reporting to the FDA may still be required, if the research is subject to FDA regulations).

3.2.2 The IRB may voluntarily report any such event to OHRP or other agencies at its discretion. All other reporting requirements described below apply regardless of funding source.

3.3 The HRPP Director and IRB Chair or designee is responsible for preparing incident reports, which include the following information:

3.3.1 The nature of the event (unanticipated problem involving risks to subjects or others, serious or continuing noncompliance, suspension or termination of approval of research);

3.3.2 Name of the institution conducting the research;

3.3.3 Title of the research project and/or grant proposal;

3.3.4 Name of the Principal Investigator on the protocol;

3.3.5 Number of the research project assigned by the IRB and the number of any applicable federal award(s)(grant, contract, or cooperative agreement);

3.3.6 A detailed description of the unanticipated problem, non-compliance, or reason for the suspension/termination including the findings of the institution and the reasons for the decision;

3.3.7 Actions the institution is taking or plans to take to address the event (e.g., revise the protocol, suspend enrollment, terminate the research, increase monitoring of subjects, etc.

3.3.8 Plans, if any, to send a follow-up or final report by the earlier of: (a) a specified date, or (b) when the investigation has been completed or a corrective action plan has been implemented.

3.4 The HRPP Director and Chair of the IRB are responsible for review and approval of the final incident report.

3.5 The report is sent to the following:

3.5.1 IRB

3.5.2 Institutional Officials

- 3.5.2.1 Vice President for Research/Director or Research (IO and Signatory of the FWA)
- 3.5.2.2 Research Compliance Officer
- 3.5.2.3 Vice President for Academic Affairs
- 3.5.2.4 Chief Corporate Compliance Officer
- 3.5.2.5 Privacy Officer, if applicable

3.5.3 Regulatory Agencies

- 3.5.3.1 OHRP [Note: As noted above, reporting to OHRP is not required unless the study is federally supported or conducted. This change is effective for studies approved (or approved with modifications) on or after February 5, 2009.]
- 3.5.3.2 FDA, if the study is subject to FDA regulations

3.5.4 Others

3.5.4.1 Principal investigator
3.5.4.2 Supervisor of the principal investigator
3.5.4.3 Any "Common Rule" Federal Agency that is supporting the research, when applicable.
3.5.4.4 The Privacy Officer of Hartford HealthCare, if the report involves unauthorized use, loss, or disclosure of individually identifiable patient information from the covered entity.
3.5.4.5 Chief Corporate Compliance Officer

3.6 The Director and Chair of the IRB or designee will ensure that all steps of this policy are completed within 30 days of the date when:

3.6.1 The IRB determines that an incident is an unanticipated problem involving risks to subjects or others;

3.6.2 The IRB determines that an incident is a serious or continuing non-compliance with Department of Health and Human Services (DHHS) or FDA regulations or the requirements or determinations of the IRB; or

3.6.3 The IRB or Institutional Official suspends or terminates IRB approved research.

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 46.116(c)(5)

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

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

5.4 Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

5.5 Guidance for Clinical Investigators, Sponsors and IRBs – *Adverse Event Reporting to IRBs – Improving Human Subject Protection*

5.6 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	General review and updating regulatory citations

Element I.5.D., II.2.G. II.2.H, and III.2.D.