1.0 Purpose:

1.1 IRB approval must be obtained prior to initiating any research activity that meets either the Department of Health and Human Services (DHHS) definition of research involving human participants or the Food and Drug Administration (FDA) definition of clinical investigation involving human participants and prior to implementing amendments to previously approved research (except when necessary to eliminate apparent immediate hazards to participants).

1.2 Before engaging in DHHS-conducted or -supported human subjects research that is not exempt under DHHS regulations 45 CFR 46.104, an institution must:

1.2.1 Hold or obtain an OHRP-approved Federalwide Assurance (FWA) 45 CFR 46.103(a); and

1.2.2 Certify to the HHS agency conducting or supporting the research that the research has been reviewed and approved by an IRB designated in the FWA and will be subject to continuing review by an IRB (45 CFR 46.103(b).

1.3 Given the above requirements, the Hartford HealthCare Human Research Protection Program (HHC HRPP) will use the following procedures to determine when HHC is considered to be engaged a proposed research activity.

2.0 Definitions:

2.1 **Research** (45 CFR 46.102(l)) - A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

2.2 **Human Subject** (45 CFR 46.102(e)) - 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.

- *Intervention* includes both physical procedures by which information or biospecimens are gathered e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- *Interaction* includes communication or interpersonal contact between investigator and subject.
- *Private information* includes 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., medical record).

2.3 **Institution** (45 CFR 46.102(f)) - Any public or private entity, or department or agency (including federal, state and other agencies). An institution's *employees or agents* refers to individuals who: (1) act on behalf of the institution; (2) exercise

institutional authority or responsibility; or (3) perform institutionally designated activities. "Employees and agents" can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

3.0 Procedure:

3.1 Institutions Engaged in Human Subjects Research

3.1.1 An institution is considered *engaged* in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain:

3.1.1.1 Data about the subjects of the research through intervention or interaction with them;

3.1.1.2 Identifiable private information about the subjects of the research; or

3.1.1.3 The informed consent of human subjects for the research.

3.1.2 An institution is considered *engaged* in a DHHS-conducted or –supported non-exempt human subjects research project (and, would need to hold or obtain OHRP-approved FWAs and certify IRB review and approval to HHS) when the involvement of its employees or agents includes any of the following:

3.1.2.1 An award is received through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e., awardee institution), even where all activities involving the subjects are carried out by employees or agents of another institution.

3.1.2.2 An institution's employees or agents intervene for research purposes with any human subjects of the research by performing invasive and non-invasive procedures. (Examples: drawing blood, administering individual or group therapy, administering drugs or other treatments; surgically implanting devices; utilizing physical sensors, etc.)

3.1.2.3 An institution's employees or agents intervene for research purposes with any human subject by manipulating the environment. (Examples: controlling light, temperature, sound, presenting sensory stimuli, etc.).

3.1.2.4 An institution's employees or agents interact for research purposes with any human subject of the research. (Examples: engaging in protocol-dictated communication; asking someone to provide a specimen by voiding or spitting into a specimen container; or conducting interviews, etc.)

3.1.2.5 An institution's employees or agents obtain the informed consent of human subjects for the research.

3.1.2.6 An institution's employees or agents **obtain** for research purposes identifiable private information or identifiable biological specimens **from any source** for the research, even if they do not directly interact or intervene with human subjects. This includes:

3.1.2.6.1 Observing or recording private behavior;

3.1.2.6.2 Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and

3.1.2.6.3 Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in possession of the investigators. (OHRP considers private information or specimens to be individually identifiable [45 CFR 46.102(f)] when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.)

3.2 **Institutions Not Engaged in Human Subjects Research**

3.2.1 An institution is considered *not engaged* in a DHHS-conducted or –supported non-exempt human subjects research project (and, would not need to hold or obtain OHRP-approved FWAs and certify IRB review and approval to HHS) when the involvement of its employees or agents in that project is **limited to one or more** of the following:

3.2.1.1 Institutions whose employees or agents perform commercial or other services for investigators provided that **all** of the following conditions are also met:

3.2.1.1.1 The services performed do not merit professional recognition or publication privileges;

3.2.1.1.2 The services performed are typically performed by those institutions for non-research purposes; and

3.2.1.1.3 The institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.

Examples: assuming the services described would not merit professional recognition or publication privileges:

- An appropriately qualified laboratory whose employees perform routine serum chemistry analyses of blood samples for investigators as a commercial service.
- A transcription company whose employees transcribe research study interviews as a commercial service.
- A hospital whose employees obtain blood through a blood draw or collect urine and provide such specimens to investigators as a service.
- A radiology clinic whose employees perform chest x-rays and send the results to investigators as a service.

3.2.1.2 Institutions (including private practices) not selected as a research site whose employees or agents provide clinical trial-related medical services that are dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (i.e., medical history, physical examination, assessment of adverse events, blood test, chest x-ray, or CT scan) provided that **all** of the following conditions are also met:

3.2.1.2.1 The institution's employees or agents **do not** administer the study interventions being tested or evaluated under the protocol;

3.2.1.2.2 The clinical trial-related medical services are typically provided by the institution for clinical purposes;

3.2.1.2.3 The institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; and

3.2.1.2.4 When appropriate, investigators from an institution engaged in the research retain responsibility for :

3.2.1.2.4.1 overseeing protocol-related activities; and

3.2.1.2.4.2 ensuring appropriate arrangements are made for reporting protocol-related data to investigators at an engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol.

Note: Institutions (including private practices) not initially selected as research sites whose employees or agents administer the interventions being tested or evaluated in the study—such as administering either of two chemotherapy regimens as part of an oncology clinical trial evaluating the safety and effectiveness of the two regimens—generally would be engaged in human subjects research (see scenario 4.2.1.3 below for a limited exception). If such an institution does not have an FWA, its employees or agents may be covered by the FWA of another institution that is engaged in the research through an Individual Investigator Agreement.

3.2.1.3 Institutions (including private practices) not initially selected as research sites whose employees or agents administer the study interventions being tested or evaluated under the protocol limited to a one-time or short-term basis (i.e., an oncologist at the institution administers chemotherapy to a research subject as part of a clinical trial because the subject unexpectedly goes out of town, or is unexpectedly hospitalized), provided that **all** of the following conditions are met:

3.2.1.3.1 An investigator from an institution engaged un the research determines that it would be in the subject's best interest to receive the study intervention being tested or evaluated under the protocol;

3.2.1.3.2 The institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research;

3.2.1.3.3 Investigators from the institution engaged in the research retain responsibility for:

3.2.1.3.3.1 overseeing protocol-related activities; and

3.2.1.3.3.2 ensuring the study interventions are administered in accordance with the IRB-approved protocol; and

3.2.1.3.3.3 ensuring appropriate arrangements are made for reporting protocol-related data to investigators at the engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol; **and**

3.2.1.3.4 an IRB designated on the engaged institution's FWA is informed that study interventions being tested or evaluated under the protocol have been administered at an institution **not** selected as a research site.

3.2.1.4 Institutions whose employees or agents:

3.2.1.4.1 Inform prospective subjects about the availability of the research;

3.2.1.4.2 Provide prospective subjects with the information about the research (which may include a copy of the relevant informed consent document and other IRB-approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators;

3.2.1.4.3 Provide prospective subjects with information about contacting investigators for information or enrollment; and/or

3.2.1.4.4 Seek or obtain the prospective subjects' permission for investigators to contact them.

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the

patient to provide the patient's name and telephone number to investigators.

3.2.1.5 Institutions (i.e., schools, nursing homes, businesses) that permit use of their facilities for intervention or interaction with subjects by investigators from another institution.

Examples of this would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes.

3.2.1.6 Institutions whose employees or agents **release** identifiable private information or identifiable biological specimens pertaining to the subjects of the research to investigators at another institution.

Note that in some cases the institution releasing the information or specimens may have requirements that need to be met before the information or specimens may be released, and/or may need to comply with other applicable regulations or laws. In addition, if the information or specimens to be released were collected for another research study covered by 45 CFR 46, then the institution releasing such information or specimens should:

a. ensure that the release would not violate the informed consent provided by the subjects to whom the information or specimens pertain (under 45 CFR 46.116), or
b. if informed consent was waived by the IRB, ensure that the release would be consistent with the IRB's determinations that permitted a waiver of informed consent under 45 CFR 46.116 (c) or (d).

Examples of institutions that might release identifiable private information or biological specimens to investigators at another institution include:

a. schools that release identifiable student test scores;
b. an HHS agency that releases identifiable records about its beneficiaries; and
c. medical centers that release identifiable biological specimens.

Note that, in general, the institutions whose employees or agents **obtain** the identifiable private information or biological specimens from the releasing institution would be engaged in human subjects research.

3.2.1.7 Institutions whose employees or agents:

3.2.1.7.1 obtain coded private information or human biological specimens from another institution involved in the research that retains a link to individually identifying information (such as name or social security number); and

3.2.1.7.2 are **unable** to readily ascertain the identity of the subjects to whom the coded information or specimens pertain because, for example:

3.2.1.7.2.1 the institution's employees or agents and the holder of the key enter into an agreement prohibiting the release of the key to the those employees or agents under any circumstances;

3.2.1.7.2.2 the releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the institution's employees or agents under any circumstances; or

3.2.1.7.2.3 there are other legal requirements prohibiting the release of the key to the institution's employees or agents.

For purposes of this document, ***coded*** means that:

a. identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, and/or combination thereof (i.e., the code); and

b. a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

3.2.1.8 Institutions whose employees or agents access or utilize individually identifiable private information **only** while visiting an institution that is engaged in the research, provided their research activities are overseen by the IRB of the institution that is engaged in the research.

3.2.1.9 Institutions whose employees or agents access or review identifiable private information for purposes of study auditing (i.e., a government agency or private company will have access to individually identifiable study data for auditing purposes).

3.2.1.10 Institutions whose employees or agents receive identifiable private information for purposes of satisfying U.S. Food and Drug Administration reporting requirements.

3.2.1.11 Institutions whose employees or agents author a paper, journal article, or presentation describing a human subjects research study.

3.3 **IRB Review Considerations for Cooperative Research**

3.3.1 Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

3.3.2 When multiple institutions may be engaged in the same non-exempt human subjects research project that is not subject to 3.3.1 (i.e., not conducted, supported, or otherwise subject to regulation by any Federal department or agency) , institutions may:

3.3.2.1 Enter into joint review arrangements;

3.3.2.2 Rely on the review of another qualified IRB; or

3.3.2.3 Make similar arrangements to avoid duplication of effort, in accordance with regulations 45 CFR 46.114.

3.3.3 When an institution is engaged in only part of a cooperative research project along the lines of 4.1.2.2 through 4.1.2.6 above, the institution must ensure that the IRB(s) designated under its FWA reviews and approves the part(s) of the research in which the institution is engaged.

For example, an institution operating the statistical center for a multi-center trial that receives identifiable private information from multiple other institutions must ensure that an IRB designated under its FWA reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center. In such a case, the IRB should ensure that the statistical center has sufficient mechanisms in place to adequately protect the privacy of subjects and maintain the confidentiality of the data.

3.3.4 When an institution is engaged in only part of a cooperative research project, the reviewing IRB may decide to review the entire research study, even if information about the entire study is not necessary to approve the institution's part of the research under 45 CFR 46.111.

4.0 References:

4.1 45 CFR 46 Subpart A – *Basic HHS Policy for Protection of Human Research Subjects*

4.2 OHRP Guidance on Engagement of Institutions in Human Subjects Research (October 16, 2008)

5.0 Documentation:

5.1 Documentation related to a formal determination by the HRPP Director that HHC is not engaged in a proposed research activity will be maintained for a minimum of three (3) years.

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

6.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
00	EHP	7/1/11	New Issue
01	CLB	3/15/20	Updates to regulatory references. Otherwise, materially unchanged.

Element I.1.A and III.1.A