1.0 Purpose:

1.1. To allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory, and where it is not possible to obtain informed consent, while establishing additional protections for participants to provide for safe and ethical studies.

1.2. To help ensure that the communities in which emergency research will be conducted and from which subjects will be drawn are adequately informed about the risks and expected benefits of the research, and are given the opportunity to ask questions about it, and express their views prior to the IRB making a determination about the research.

1.3. This policy outlines those steps the Hartford HealthCare Human Research Protection Program (HHC HRPP) and Institutional Review Board (IRB) will take to ensure that these objectives are fulfilled.

2.0 Definitions:

2.1 Community Consultation - Providing the opportunity for discussion with, and soliciting opinions from, the community in which the study will take place and the community from which the study subjects will be drawn.

2.2 Community in which Research will be Conducted - The geographic area or city or region where the study site is located, as well as the area served by the site through health care providers affiliated with the site and the area covered by emergency medical technicians, paramedics, and first responders.

2.3 Community from which Subjects will be Drawn - The population at risk; that is, the group of patients who share a particular medical or other characteristic that increases the likelihood that they (or a family member) may be enrolled in the study.

2.4 Emergency Research - A planned clinical investigation that requires prior written FDA authorization to proceed, and involves subjects who are in a life-threatening situation for which available treatments or *in vitro* diagnostic tests are unproven or unsatisfactory.

2.5 Legally Authorized Representative (LAR) - An individual or judicial or other body authorized under applicable State or local law to give informed consent on behalf of a prospective subject to the subject's participation in procedure(s) involved in the research.

2.6 Public Disclosure - Dissemination of information to the community, the public, and researchers about the emergency research prior to the research in sufficient detail to allow a reasonable assumption that the community is aware of the plans for the investigation, its risks and expected benefits, and that the study will be conducted without obtaining informed consent from most or all participants; and after the research in sufficient detail to make the community aware of the study's results.

2.7 Treatment Window - The time period during which administration of the test article might reasonably produce a demonstrable clinical effect, or for *in vitro* diagnostic devices, the time period during which diagnosis must occur to allow administration of appropriate therapy.

3.0 Procedures:

3.1 **Prepare Materials to Notify and Consult with the Community**

4.1.1 Letter to research community panel describing the study.

4.1.2. Questionnaire for panel members' responses.

4.1.3. Proposed method(s) of notifying the community and content of the notification.

4.1.4. Procedures for public disclosure following completion of the study.

4.1.5. Regular IRB submission materials (Research Application, protocol, etc.).

3.2 **Submit the Prepared Materials for IRB Review**

3.2.1 Include a cover letter outlining why waiver of consent is appropriate for this study and how the consent process will be attempted and documented.

3.3 **After IRB Approval**

3.3.1 Before patients may be enrolled under the waiver of consent, the investigator must:

4.3.1.1. Provide the IRB with the INDD/IDE number issued by the FDA for the emergency research waiver. This will be an IND/IDE specifically for this purpose and is in addition to the IND/IDE to conduct the study.

4.3.1.2. Notify the public using the method(s) approved by the IRB.

4.3.1.3. Attempt, at the earliest point possible, to obtain informed consent from the patient or other representative during the treatment window, prior to the research intervention, and to document these attempts.

4.3.1.3.1. Consent should be obtained from individuals in the following order:

- Patient
- Legally authorized representative (LAR) if the patient is not able to provide consent
- A family member, if the LAR is not available, should be asked whether he or she objects to the patient's participation

4.3.1.3.2. As soon as possible, the investigator must inform the patient, LAR, or family member of the patient's inclusion in the study, the details of the research, and other information contained in the

informed consent document, and conduct the informed consent process.

4.3.1.3.3. Repeated attempts must be made to obtain consent from the patient, LAR, or family member in the following order:

- Patient
- If the patient remains incapacitated, and informed consent was not already obtained from an LAR or family member, then the investigator must attempt to obtain informed consent in the following order:
  - LAR
  - Family member
- If the patient remains incapacitated, and a family member's permission was obtained, the investigator must attempt to obtain informed consent from the LAR.
- If the patient becomes capable of providing consent, the investigator must attempt to obtain informed consent from the patient.

4.3.1.3.5. The investigator must maintain documentation of the attempts to obtain informed consent from the patient, LAR, and family member. A summary of these attempts must be provided to the IRB at the time of continuing review.

4.3.1.3.4. The patient, LAR, or family member has the right to withdraw the patient from the study without any penalty or loss of benefits to the patient.

4.3.1.3.5. If a patient is entered into the research with waived consent, and the patient dies before an LAR or family member can be contacted, information about the clinical investigation is to be provided to the patient's LAR or family member, if feasible.

4.4 After Completion of the Study

4.4.1. The investigator must notify the public of the research study, including demographic characteristics of the study population and the study results.

4.5 Emergency Research Waiver Criteria – The HC IRB is responsible for review, approval, and continuing review of planned emergency research. In order to approve such research without requiring that informed consent of all research be obtained, it must find and document that each of the following criteria are satisfied. The IRB must obtain the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation.

4.5.1. The human subjects are in a life-threatening situation.

4.5.2. Available treatments are unproven or unsatisfactory and

4.5.3. The collection of valid scientific evidence (which may include evidence obtained from randomized placebo-controlled investigations) is necessary to determine the safety and effectiveness of the proposed intervention.

4.5.4. Obtaining consent is not feasible because

4.5.4.1. The subjects will not be able to give informed consent as a result of their medical condition

4.5.4.2. The intervention under investigation must be administered before consent from the subjects' legally authorized representative if feasible AND

4.5.4.3. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

4.5.5. Participation in the research holds out the prospect of direct benefit to the subjects because

4.5.5.1. Subjects are facing a life-threatening situation that necessitates intervention

4.5.5.2. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects and

4.5.5.3. Risks associated with the proposed research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

4.5.6. The research could not practically be carried out without the waiver.

4.5.7. The proposed plan defines the length of the potential treatment window based on scientific evidence, and

4.5.8. The investigator has committed to attempting to contact a legally authorized representative (LAR) for each subject within that window of time and, if feasible, to asking the LAR for consent within that window rather than proceeding without consent.

4.5.9. The investigator will summarize efforts made to contact LARs and make this information available to the IRB at the time of continuing review.

4.5.10. The investigator commits to using the informed consent procedures and informed consent document approved by the IRB with subjects or their

LAR in situations where use of such procedures and documents is feasible.

4.5.11. The IRB must be provided with and approve the procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research.

4.5.12. Additional protections of the rights and welfare of the subjects will be provided, including at least:

4.5.12.1. Consultation with representatives of the communities in which the research will be conducted and from which the subjects will be drawn (including, where appropriate, consultation carried out by the IRB).

4.5.12.2. Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits.

4.5.12.3. Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population and its results.

4.5.12.4. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation and

4.5.12.5. If obtaining informed consent is not feasible, and an LAR is not reasonably available, the investigator has committed, if feasible, to attempting to contact the subject's family member who is not an LAR, within the treatment window, and asking whether he or she objects to the subject's participation in the research.

4.5.12.6. The investigator will document efforts to contact family members and make this information available to the IRB at the time of continuing review.

4.5.13. For research subject to FDA regulations, the research must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that my include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug or IDE for the same device already exists.

4.5.13.1. The IND/IDE holder must be willing to allow the enrollment of individuals without informed consent.

4.5.13.2 The IND/IDE holder must confirm with the FDA that the enrollment of individuals without informed consent will be allowed for this study.

4.5.14. If the research is not subject to FDA regulations, but is federally funded, documentation that the above criteria have been met will be sent to the Office for Human Research Protections (OHRP). The research will not be allowed to begin until OHRP has concurred that the waiver is appropriate.

4.5.15. If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria for the exception from informed consent requirements, or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation, including reasons for this determination.

4.6. Community Consultation

4.6.1. The goals of community consultation are:

4.6.1.1. To show respect for persons by informing the community about the study in advance;

4.6.1.2. To provide a means for affected communities to provide meaningful input to the IRB before its decision to approve, require modifications to, or disapprove the study;

4.6.1.3. To show respect for the community by allowing representatives of the community to identify potential community-level concerns and effects of the research; and

4.6.1.4. To show respect for subjects' autonomy, for example, by including in community consultation activities individuals who may have, or be at risk for, the condition under study.

4.6.2. During community consultation, the sponsor and clinical investigator(s) should:

4.6.2.1. Inform the communities that it is proposed that informed consent will not be obtained for most (or all) research subjects, including an explanation as to why consent is not feasible;

4.6.2.2. Inform the communities about all relevant aspects of the proposed study, including its risks and expected benefits;

4.6.2.3. Hear and respond to the perspective of the communities on the proposed research; and

4.6.2.4. Provide information about ways, if any, in which individuals wishing to be excluded may indicate this preference.

4.6.3. At a minimum, the following information should be included in community consultation:

- A summary of the research protocol, study design, and a description of the procedures to be followed, including the identification of any procedures which are experimental;

- A summary of other available treatment options and what is known about their risks and benefits;
- An estimate of how long the study will last and expected duration of the subject's participation;
- How potential study subjects will be identified;
- Information about the test article's use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
- A clear statement that informed consent will not be obtained for most research subjects;
- The rationale as to why the study must be conducted using an exception from informed consent;
- A copy of the informed consent document;
- Relevant information that would be part of the informed consent process (21 CFR 50.25(a) and (b), as applicable), e.g., available treatments for the condition under study; risks/potential benefits of participating in the research; possibility that FDA might inspect the subject's records;
- A description of the treatment window, during which the test article must administered, and the portion of that window that will be used to contact the subject's LAR;
- A description of the attempts that will be made to contact the subject's LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject's enrollment in the study, both before and after the test article is administered (See Questions 38-43);
- A description of the way(s) in which an individual may express his/her desire not to participate and avoid involvement as a subject in the research (e.g., opt-out mechanisms), if any will be made available (See Questions 37 and 68);
- Reasons why community input is important;
- Known community perceptions/concerns associated with the study, product, and/or standard of care; and
- Identification of individuals to contact for more information about the study.

4.6.4. The following factors also should be considered:

- protocol design (e.g., whether the investigational product is substituted for or added to standard of care);
- what is known about the test article (e.g., FDA approved, available safety or toxicity information, product history including extent of use, approval in another population or for another indication, scientific evidence from other countries);
- what is known about the medical condition;
- what is known about the safety and efficacy of "standard of care" (i.e., why existing, available treatments are considered unproven or unsatisfactory);
- study population (e.g., adults vs. pediatric population);
- characteristics of the setting in which the test article will be administered (e.g., will the product first be administered in the ambulance by EMTs or in the ER, will the product be continued in the ER, what is the availability of resources, what training will be provided to personnel who will be involved with the research)

- timing of administration of the test article;
- invasiveness of procedures necessary to administer the product;
- perceived availability or acceptability of alternative treatments.

4.6.5. The IRB should consider the community's opinions and concerns, assess the consultation process, and incorporate the results of community consultation and discussion into its decision making by:

4.6.5.1. Reviewing, requesting appropriate modifications in, and approving or disapproving the plans for community consultation;

4.6.5.2. Assessing the adequacy of the community consultation;

4.6.5.3. Considering the community concerns and incorporating the feedback, as appropriate, into its review of the protocol and informed consent document;

4.6.5.4. Reflecting consideration of community consultation in the meeting minutes.

4.6.6. Community consultation activities include, but are not limited to, the following:

4.6.6.1. Standing meetings, such as local civic public forums;

4.6.6.2. Public community meetings or other special meetings which may be specifically organized to discuss the research;

4.6.6.3. Local radio and/or television talk shows;

4.6.6.4. Interactive websites, focus groups and surveys.

4.6.7. The number of consultation activities and the number of participants needed to fulfill these requirements may vary, and should be based on factors such as the size of the communities, the languages spoken within those communities, the targeted research population and its heterogeneity.

4.7. Public Disclosure

4.7.1. Public disclosure is required both before the research may begin and after it has been completed. The IRB must document that public disclosure has occurred.

4.7.2. The goal of public disclosure prior to the research is to provide sufficient information to allow a reasonable assumption that the community is aware of the plans for the investigation, its risks and expected benefits, and that the study will be conducted without obtaining informed consent from most study subjects.

4.7.3. Information that should be disclosed prior to the study includes:

- A summary of the research protocol, study design and a description of the procedures to be followed, including identification of any procedures which are experimental;
- A summary of other available treatment options and what is known about their risks and benefits;
- An estimate of how long the study will last and expected duration of the subject's participation;
- How potential study subjects will be identified;
- Information about the test article's use, including a balanced description of the risks and expected benefits and any relevant information that is known about adverse events;
- A clear statement that informed consent will not be obtained for most research subjects;
- The rationale as to why the study must be conducted using an exception from informed consent;
- A copy of the informed consent document;
- A description of the attempts that will be made to contact the LAR to obtain consent, or, if no LAR is available, a family member to provide an opportunity to object to the subject's enrollment in the study, both before and after the test article is administered (See also Questions 38-43);
- If the IRB determines that an opt-out mechanism is appropriate and feasible, a description of the way(s) in which members of the community may communicate a decision not to participate in the study (e.g., use of medical identification bracelets or wallet cards, annotation on driver's license) (See also Questions 37 and 68);
- The sites or institutions that will be participating in the research;
- Community perceptions/concerns with the study, product, and/or standard of care that were raised during community consultation and any associated modifications that were made to the research; and
- Identification of individuals to contact for more information about the study.

4.7.4. The goal of public disclosure after the research is to ensure that the community, the public, and researchers are aware of the study's results. It is recommended that disclosure occur within one year of completion or termination of the study.

4.7.5. Information that should be disclosed after the study should provide sufficient detail to allow a clear understanding of the study design and its results, both positive and negative, and should include:

- Demographic characteristics of the research population
- Primary outcomes of the study
- The number and nature of adverse events associated with the test article
- Whether the study was terminated, and if so, the basis for that decision.

4.7.6. The IRB may determine that additional disclosure during the study is appropriate, if, for example, new information becomes available during the study. Any such disclosures should be made promptly.

4.7.7. Public disclosure may be carried out via multiple venues. Applicable clinical trials must be registered at http://www.clinicaltrials.gov. Other possible disclosure activities include:

- targeted mailings to households in the communities, with information about how to obtain further details;
- advertisements and articles in the English language, and if appropriate, foreign language, newspapers (Public outreach documents should be translated into languages that are common in the area served by the facility where the investigation is being conducted and in the communities from which subjects will be drawn.);
- clearly marked links and information on the sponsor's and participating hospitals' Internet web sites;
- summary materials that are accessible to non-English speaking or homeless populations who reside in the community from which research subjects are likely to be drawn;
- presentation or distribution of information at meetings of community, local government, civic, or patient advocacy groups;
- letters to local and regional community leaders and first responders (e.g., police, paramedics);
- announcements to local/regional hospital staff(s);
- public service announcements and interviews or discussions on "talk" radio or television programs;
- press conferences and briefings; and
- meetings or activities provided by hospitals' and institutions' existing community outreach programs.

4.7.8. The following disclosure activities, either by themselves or in combination, do not satisfy the public disclosure requirements:

- A legal notice
- Letter to physicians
- Informing staff at the site where the research will take place

4.0 Documentation:

4.1 The HHC HRPP office will maintain the IRB determinations required by this policy for a period of six (6) years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by the FDA or other appropriate authority.

5.0 References:

5.1 21 CFR 50.24

5.2 45 CFR 46.116(f)

5.3 ICH-GCP 3.1.7, 4.8.15

5.4 DEPARTMENT OF HEALTH AND HUMAN SERVICES, 45 CFR Part 46 Waiver of Informed Consent Requirements in Certain Emergency Research (Federal

Register, Vol. 61, No.192, October 2, 1996)
http://www.hhs.gov/ohrp/documents/100296.pdf

5.5 Emergency Research Informed Consent Requirements (OPRR Letter, 1996) - http://www.hhs.gov/ohrp/policy/hsdc97-01.html

5.6 FDA Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors - Exception from Informed Consent Requirements for Emergency Research (March 2011)
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf

6.0 Attachment

6.1 Figure 2: Decision Tree for Obtaining Informed Consent under Emergency Research Waiver of Informed Consent

7.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
01	SMH	7/1/11	Conversion to new policy template; general expansion of policy
02	CLB	3/15/20	General review

Elements II.4.C

Decision Tree for Obtaining Informed Consent under Emergency Research Waiver of Informed Consent

Figure 2