1.0 Purpose:

1.1 To support physicians/researchers needing to implement the emergency use provisions allowed under the Food & Drug Administration (FDA) regulations, this policy clarifies and outlines the necessary requirements and procedures to ensure full compliance with those regulations and protection of subjects.

2.0 Definitions:

2.1 **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 312 (new drug applications) of the Federal Food, Drug, and Cosmetic Act (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.

2.2 **Compassionate Use -** The treatment of a seriously ill patient using an unapproved test article where no other available treatments are satisfactory. Such use of an investigational drug, device, or biologic actually falls into one of the following treatment mechanisms and is allowed only after prior review and approval by the HHC IRB, and in most circumstances prior approval by the FDA as well. FDA guidance includes limited provisions for compassionate use in serious, but not life-threatening, situations. Prior IRB approval is needed even if only one patient is to be treated under the following mechanisms of **"Expanded Access:"**

2.2.1 **Treatment INDs or Individual Patient Access to Investigational Drugs/Devices -** These mechanisms are primarily intended to give seriously ill patients access to experimental drugs or devices where no comparable or satisfactory alternative treatment is available. Although the test article sponsor is expected to continue conventional clinical trials and pursue marketing approvals with due diligence, expanded access studies involve systematic use of experimental treatments, and, with very rare exceptions, require the same review and approval as research, including both IRB approval and FDA approval in the form of an IDE (medical device) or an IND (drug/biologic).

2.2.2 **Open Protocols (Parallel Track, Open Label Protocol, Open Label IND) or Continued Access IDEs -** Uncontrolled studies, typically used when controlled trials have ended and treatment is continued so the subjects may continue to receive the benefits of the test article until marketing approval is obtained. Informed consent and prior HHC IRB approval are required.

2.3 **Emergency Use (Drug or Biologic) -** The use of an investigational (or unapproved) drug or biologic product for a human subject "in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain" HHC IRB approval (21 CFR 56.102(d)). The emergency use provision of the FDA regulations (21 CFR 56.104(c)) is an exemption from prior review and approval by the IRB. However, reporting the use to the IRB is required by the FDA. The exemption may not be used unless **ALL** of the conditions previously mentioned exist. Generally, emergency use of an unapproved drug or biologic requires an IND. However, emergencies may arise where an unapproved device may offer the only

possible life-saving alternative, but an IND for the drug or biologic does not exist, or the proposed use is not approved under an existing IND, or the physician or institution is not approved under the IND.

2.4 **Emergency Use (Device):** The use of an unapproved device (for a human subject) for a purpose or condition for which the device requires, but does not have, an approved application for pre-market approval (FDA approval of marketing). An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an investigational device exemption (IDE). However, emergencies may arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE.

2.5 **Human Subject -** A living individual (1) about whom an investigator (whether professional or student) conducting research obtains either (a) data through intervention or interaction with the individual; or (b) identifiable private information; or (2) who is or becomes a participant in research involving drugs or devices, either as a recipient of a test article or as a control. Note that both human subject and human participant are used interchangeably in IRB policies and procedures. While the term "participant" conveys the voluntary nature of an individual's agreement to participate in the research, it also can convey a sense of partnership, which is not reflected in all types of research. In some cases, the research volunteer is in fact more acted upon than truly having any sense of partnership in the research. Hence, the term subject is considered more appropriate in such cases.

2.6 **Investigational Device Exemption -** Under FDA regulations (21 CFR 812), research that is conducted to determine the safety or effectiveness of a device must have an Investigational Device Exemption (IDE) issued by the FDA. The FDA will place all IDEs it approves in one of two categories:

2.6.1 **Category A – Experimental:** The IDE involves innovative devices in which "absolute risk" has not been established (i.e., initial questions of safety and effectiveness have not been resolved and thus FDA is unsure whether the device type can be safe and effective)

2.6.2 **Category B – Investigational; Non-experimental:** The clinical investigation involves device types believed to be in classes I or II or device types believed to be in class III where the incremental risk is the primary risk question (i.e., underlying questions of safety and effectiveness of that device type have been resolved). This category includes device types that can be safe and effective because, for example, other manufacturers have obtained FDA approval for that device type. Nonsignificant risk studies may also be included in this category.

2.7 **Investigational New Drug (IND) application -** An exemption from the FDA premarketing requirements that are otherwise applicable which allows the drug to be shipped lawfully for the purpose of conducting clinical investigations of the drug. Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will usually ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA. There are three additional IND types and two categories:

2.7.1 **IND Types**

2.7.1.1 Investigator IND (Sponsor-Investigator): An investigator IND is submitted to the FDA by an investigator who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed

2.7.1.2 Treatment IND: A treatment IND is submitted to the FDA to make promising new drugs available to desperately ill patients as early in the drug development process as possible. FDA will permit an investigational drug to be used under a treatment IND if there is preliminary evidence of drug efficacy and the drug is intended to treat a serious life-threatening disease in its later stage of development or if there is no alternative drug or therapy available to treat that stage of the disease in the intended individuals.

2.7.1.3 Emergency Use IND: The Emergency Use IND allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND in accordance with the regulations. It is also used for patients who do not meet the criteria for an existing study protocol, or if an approved study protocol does not exist.

***NOTE:** Emergency and Treatment INDs are sometimes referred to as "Compassionate Use" INDs, but the term "Compassionate Use" is not in the IND regulations.

2.7.2 **IND Categories**

2.7.2.1 Commercial - These are applications that are submitted primarily by companies whose ultimate goal is to obtain marketing approval for a new product

2.7.2.2 Research (non-commercial)

2.8 **Life threatening -** In the Emergency Use context, life-threatening means a high likelihood of death unless the course of the patient-participant's condition or disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. Immediacy of death is not required. "Life-threatening" in this context also includes "**severely debilitating**" circumstances, i.e., diseases or conditions that cause major irreversible morbidity (e.g., blindness, loss of arm, leg, hand, or foot, loss of hearing, paralysis or stroke).

2.9 **Sponsor-Investigator -** Sponsor-Investigator is an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the investigational drug or device is administered, dispensed, or used. The term does not, for example, include a corporation or agency. The obligations of the sponsor-investigator include those of an investigator and those of a sponsor.

2.10 **Sufficient time to obtain IRB approval -** If the decision that the test article is needed is made 5 working days or more prior to a scheduled meeting of any of the two IRBs and if the meeting will occur before use of the test article is necessary

(according to the treating physician's judgment of when use of the test article is necessary), this is considered to be sufficient time to obtain IRB approval.

2.11 **Test Article -** An unapproved FDA-regulated product (i.e., unapproved drug, device, or biologic)

3.0 Procedure:

3.1 Requirements for Drugs, Biologics, and Devices

3.1.1 All of the following conditions must be met for this type of emergency use:

3.1.1.1 A patient is in a life-threatening situation/condition that needs immediate treatment

3.1.1.2 There is no standard/generally acceptable alternative for treating the patient available

3.1.1.3 Because of the immediate need, there is no time to use existing procedures to obtain IRB and FDA approval for the use.

3.2 Regulatory Requirements for Drugs or Biologics

3.2.1 **FDA Permits one emergency use of an unapproved drug or biologic per institution without prospective IRB review and approval (21 CFR 56-104(c)).** FDA requires that any subsequent use of the investigational product at the institution have prospective IRB review and approval. If it appears probable that similar emergencies will require subsequent use of the test article at Hartford HealthCare (HHC), the investigator is advised to make every effort to develop a protocol for future use of the article at HHC. The study will require prospective review and approval by the IRB. **IMPORTANT NOTE:** FDA guidance acknowledges that it would be inappropriate to deny an unapproved drug or biologic to a second individual if the only obstacle is that the IRB had not had sufficient time to convene a meeting to review the second use. In cases at HHC where the IRB does not have sufficient time to convene, a determination regarding acceptability of the second use of an unapproved drug or biologic in an emergency situation must be made by the IRB Chair.

3.2.2 **Emergency use of an unapproved drug or biologic requires an Investigational New Drug (IND) exemption.** This may be accomplished in one of three ways:

3.2.2.1 The physician identifies an existing protocol for the same test article that is already approved by the HHC IRB and for which the patient may be enrolled and is able to provide consent according to the requirements of the protocol and its IRB approval. In this case, the emergency use procedure is not needed. If an enrollment exception is needed in order to enroll the patient, the study PI should consult with the sponsor.

3.2.2.2 The physician should communicate with the holder of an IND for the product (such as the manufacturer) to ascertain whether the emergency use may occur under an existing IND and the IND holder is willing to provide the test article.

3.2.2.3 If the use may not occur under an existing IND, but the IND holder is willing to provide the test article, the physician must obtain an IND from the FDA. If the situation does not allow time for submission of an IND, the FDA may issue an authorization of shipment in advance of an IND.

3.2.3 **The physician must obtain the consent of the patient or a legally authorized representative,** or else determine that the emergency use meets the criteria for an exception to the requirement of consent. (See Section 3.4 below). If consent is sought from the prospective recipient or the recipient's legally authorized representative, it will be obtained in accordance with FDA regulations and would be appropriately documented in accordance with FDA regulations.

3.2.4 **The physician must file a report with the IRB within 5 working days** after use of the test article. This report should contain a summary of the conditions constituting the emergency, patient outcome information, and the patient protection measures that were followed.

3.2.5 **Subsequent to the emergency use, the physician should evaluate the potential for future use of the test article at HHC** and, if necessary, initiate efforts to obtain IRB approval and regulatory clearance of the unapproved drug or biologic for such future uses.

3.3 **Regulatory Requirements for Devices**

3.3.1 **FDA permits one emergency use of an unapproved device without prospective IRB review and approval.** The FDA requires that any subsequent use of the investigational product at HHC have prospective IRB review and approval.

3.3.2 **FDA requires that use of an unapproved device occur under an Investigational Device Exemption (IDE).** The physician should communicate with the holder of an IDE for the product (such as the manufacturer) to ascertain whether the emergency us may occur under an existing IDE or if the physician must obtain an IDE from the FDA.

3.3.2.1 If there is no IDE for the device, or if the proposed use, the treating physician, or HHC are not approved under an existing IDE, a device may be used without FDA approval ***if*** there is an immediate need to use the device and there is no time to use existing procedures to get FDA approval for use of the device. The manufacturer or physician must notify the FDA immediately after shipment of the device to HHC and again in writing after use.

3.3.2.1.1 The FDA expects the physician to assess the potential for benefits from the unapproved use of the device and to have substantial reason to believe that benefits will exist.

3.3.2.1.2 The FDA advises that the physician may not conclude that an "emergency" exists based solely on the expectation that the IDE approval procedures may require more time than is available. The FDA expects physicians to exercise reasonable foresight with respect to potential emergencies and to make appropriate procedures under IDE procedures far enough in advance to avoid creating a situation constituting an emergency.

3.3.2.2 **Subsequent emergency use of an unapproved device may not occur unless** the physician or another person obtains FDA approval of an investigational Device Exemption (IDE) for the device and its use. If the FDA disapproves an IDE application for subsequent uses, the device may not be used again even if the circumstances constituting an emergency exist.

3.3.3 **The FDA expects the physician to obtain as many of the following protections as possible:**

3.3.3.1 An independent assessment by an uninvolved physician (at HHC, this may be the IRB Chair or another qualified physician designee);

3.3.3.2 Informed consent from the patient or their legally authorized representative (See Section 3.4 below);

3.3.3.3 Clearance from HHC other institutional officials as specified by HHC policies;

3.3.3.4 Concurrence of the IRB Chair; and

3.3.3.5 Authorization from the IDE holder if an approved IDE for the device exists

3.3.4 **After an unapproved device is used in an emergency, the physician should:**

3.3.4.1 Report to the IRB within **5 working days**

3.3.4.2 Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for subsequent use; and

3.3.4.3 Report to the FDA **within 5 working days** (if there is an IDE, the physician should provide the necessary information to the IDE sponsor so that the IDE sponsor may report to the FDA). This report should contain a summary of the conditions constituting the emergency, patient outcome information, and patient protections measures that were followed.

3.4 **Regulatory Requirements Regarding Informed Consent for Emergency Use**

3.4.1 Except as outlined below, physicians are required to obtain legally effective informed consent for the emergency use of a test article. FDA requirements for legally effective informed consent are detailed in 21 CFR 50.20, 50.25 and 50.27.

3.4.2 FDA regulations at 21 CFR 50.23(a) provide for an exception from general requirements for informed consent if the treating physician and a physician not otherwise involved in the emergency use (at HHC, the IRB Chair or another qualified physician designee), certify in writing that all of the following criteria are met:

3.4.2.1 The prospective recipient is confronted by a life-threatening situation necessitating the use of the test article.

3.4.2.2 Informed consent cannot be obtained from the recipient because of an inability to communicate with, or obtain legally effective consent from, the recipient.

3.4.2.3 Time is not sufficient to obtain consent from the recipient's legal representative.

3.4.2.4 There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the recipient.

3.4.3 If immediate use of the test article is, in the treating physician's opinion, required to preserve the life of the recipient, and time is not sufficient to obtain independent certification of the criteria listed above in advance of using the test article, the determinations of the treating physician shall, within 5 working days after the emergency use, be reviewed and evaluated in writing by a physician who is not otherwise involved in the emergency use (at HHC, the IRB Chair or another qualified physician designee).

3.5 **Researcher/Physician's Responsibilities**

3.5.1 Physicians are encouraged to obtain consultation from an HHC HRPP/IRB Chair prior to the emergency use of a test article, whenever possible.

3.5.2 Physicians should attempt to identify any protocols already approved by the HHC IRB using the same test article for which either the patient might qualify or the sponsor would grant an exception to the inclusion/exclusion criteria.

3.5.3 Physicians are responsible for confirming that there has not been a prior emergency use of the test article at HHC. However, if the product is a drug or biologic and has been used previously, a second use may be allowed if the IRB Chair (or designee) provides the determination described in Section 3.1.1 above.

3.5.4 Physicians must submit the "*Request for Emergency/Compassionate Use of Unapproved Test Article*" Form to the IRB office. This form is available on the HHC Research website.

3.5.5 Physicians are responsible for obtaining an independent assessment and approval from the IRB Chair or designee. The IRB Chair's designee should provide the assessment and approval if the IRB Chair is involved in the patient's care or if the IRB Chair is unavailable.

3.5.6 Physicians are responsible for identification of and compliance with any institutional policies regarding receipt, dispensing, use and/or control of test articles.

3.5.7 Subsequent to the emergency use, the physician should evaluate the potential for future use of the test article at HHC and, if necessary, initiate efforts to obtain IRB approval and regulatory clearance (IND or IDE) for such future uses.

3.5.8 Physicians are responsible for ensuring that the patient is not included in a systematic investigation designed to develop or contribute to generalizable knowledge.

3.5.8.1 This above provision does not limit the provision of outcomes or safety information as required by the FDA.

3.5.8.2 The above provision does not preclude the retrospective use of data (under appropriate IRB review and approval for such a study).

3.5.8.3 The above provision does not preclude the use of information in publication or presentation of a case history. When publishing or presenting more than one case, please contact HRPP to ascertain whether this constitutes human recipients research requiring IRB review and approval.

3.5.9 **Physicians are required to submit a report to the IRB <u>within 5 working days</u> of administering the test article.**

3.6 **IRB Responsibilities**

3.6.1 The HRPP/IRB will respond to physician inquiries prior to the emergency use of a test article, and will provide appropriate advice and counsel as to the acceptability of proceeding with the proposed activity.

3.6.2 The HRPP/IRB will maintain a list of test articles used according to emergency use guidelines. A list derived from the database will be available from the HRPPDirector for consultation by physicians. The list will be updated after each emergency use of a test article reported to the HHCIRB.

3.6.3 The IRB Chair will determine whether the treating physician met FDA regulations and guidance.

3.6.3.1 In instances where the IRB Chair has been involved in the care of the patient, or serves as the IRB Chair (or designee), an alternate physician member of the IRB will review the physician's report.

3.6.3.2 The IRB Chair or designee will document his/her review of the report on the emergency use checklist provided with the physician's report.

3.6.4 The IRB Chair or designee, with assistance from the HRPP staff, will communicate any questions or concerns to the physician in writing.

3.6.5 The IRB's receipt of the notification of an Emergency Use and the Chair's review is neither an IRB approval nor an indication that the specific use was prospectively reviewed by the IRB. Formal approval of a protocol requesting the use of an investigational product may only be obtained through full IRB review.

3.6.6 Non-compliance with emergency use requirements will be processed following HRPP policies and procedures for noncompliance.

3.6.7 If the IRB Chair or designee determines that the report requires notification to or review by the convened Board, HRPP staff will prepare the report for discussion at the next scheduled IRB meeting, and add the report to the meeting agenda.

3.6.8 The IRB will receive, review, and file physicians' reports following administration of the test article. The HRPP will maintain documentation of all emergency use reports submitted to the IRB.

3.7 **HHC IRB Chair Responsibility**

3.7.1 The HHC IRB Chair is responsible for providing physicians with an independent assessment and approval for the emergency use of a test article and, if applicable, for the exception to the informed consent requirement. The IRB Chair's designee should provide the assessment and approval if the IRB Chair is involved in the patient's care**.**

3.7.1.1 The IRB Chair (or designee) shall document his or her determinations on the same checklist as the treating physician and sign and date where required.

3.7.1.2 If the emergency use proceeds without informed consent without the determinations of the IRB Chair (or designee) (see Section 3.4.2 above), such determinations must be obtained within 5 working days after the emergency use.

3.7.2 In cases where an unapproved drug or biologic has previously been used in an emergency at HHC, but the IRB has not had sufficient time to convene a meeting to review the issue, the IRB Chair (or a designee if the IRB Chair is involved in the care of the patient) must make a prospective determination regarding the acceptability of a second use of the test article in an emergency situation.

3.7.2.1 The IRB Chair or designee must determine that although the test article has been used at HHC in a previous emergency, there is insufficient time to obtain IRB review and approval for the second emergency use.

3.7.2.2 The determination must also include justification for the additional use.

3.7.2.3 The determination must be made prior to the emergency use.

3.7.2.4 A written statement of the determinations regarding second use, signed and dated by the IRB Chair or designee, must accompany the physician's post-use report to IRB/HRPP.

3.8 **Treatment Use of an Investigational or Unlicensed Drug or Device**

3.8.1 An investigational drug or device may be used in a research study (clinical investigation) for the treatment (or diagnosis) of a serious or immediately life-threatening disease or condition inpatients for whom no comparable or satisfactory alternative drug, device, or other therapy is available. During the course of the research study, it may be appropriate to use the drug or device in the treatment of a patient not able to enroll in the research, in accordance with a specially developed treatment protocol or treatment IND or IDE (21 CFR 312.34 and 812.36).

3.8.2 The provider in this case is regarded as a treating physician for the patient, and not an investigator for a research participant. The physician is required to develop and submit a specific protocol application and associated consent document for full IRB review and approval prior to the specifically intended single-patient treatment use of an IND or IDE. The physician should seek FDA approval for the treatment use of an IND or IDE before requesting IRB review. Treatment may begin 30 days after FDA receives the treatment IND or IDE submission, or on earlier notification by FDA that the treatment use described in the protocol may begin, unless FDA notifies the sponsor in writing earlier than the 30 days that the treatment use may not begin.

3.8.3 **Criteria for Treatment IND or Treatment IDE**

3.8.3.1 FDA will permit an investigational drug or device to be used for a treatment use under a treatment protocol or treatment IND (or IDE) if the physician/investigator provides sufficient evidence of safety and effectiveness to support such use, or provides reasonable basis that the drug or device may be effective for its intended use in its intended patient population; or would not expose the patients to whom the drug is to be administered to an unreasonable and significant additional risk of illness or injury. The physician/investigator must demonstrate that:

3.8.3.1.1 The drug (or device) is intended to treat (or diagnose) a serious or immediately life-threatening disease (or condition);

3.8.3.1.2 There is no comparable or satisfactory alternative drug (or device) or other therapy available to treat (or diagnose) that stage of the disease (or condition) in the intended patient population;

3.8.3.1.3 The drug (or device) is under investigation in a clinical trial under an IND in effect for the trial (or for

the same use under an approved IDE), or all clinical trials have been completed; and

3.8.3.1.4 The sponsor of the clinical trial (or investigation) is actively pursuing marketing approval (or clearance) of the investigational drug (or device) with due diligence.

3.8.3.2 To ensure that appropriate safeguards are in place, treatment use of an investigational drug (or device) is conditioned on the sponsor and physician/investigator complying with the safeguards of the IND (or IDE) process, including the regulations governing informed consent and prior review and approval by the IRB, and the provisions of 21 CFR 312 (or 21 CFR 812) that include distribution of the drug (or device) through qualified experts, maintenance of adequate manufacturing facilities, and submission of IND (or IDE) safety reports.

3.9 **Compassionate Use of an Investigational or Unapproved Device**

3.9.1 For devices only, FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious, albeit not life-threatening condition (referred to as "compassionate use"). In these circumstances, FDA uses its regulatory discretion in determining whether such use of an investigational device should occur. Unlike emergency use of an unapproved device, prior FDA approval **IS** needed before compassionate use occurs. In order to obtain FDA approval, the sponsor should submit an IDE supplement requesting approval for a protocol deviation under section 812.35(a) in order to treat the patient.

3.9.2 Use of Investigational New Drugs and Devices in Human Research, the FDA allows for those situations in which an investigational or unapproved device is needed to save the life of a patient or to prevent irreversible morbidity. The FDA recognizes, however, that there are circumstances in which an investigational device is the only option available for a patient faced with a serious, albeit not life-threatening condition (referred to as "compassionate use" of the device). (Note on the term, “Compassionate Use” -- Emergency and Treatment INDs are sometimes referred to as "Compassionate Use" INDs, but the term "Compassionate Use" is not in the IND regulations; it is only in the IDE regulations.) In these circumstances, FDA uses its regulatory discretion in determining whether such use of an investigational device should occur. Accordingly, a physician who wishes to use an investigational device for compassionate use in treating a patient will need to request the device sponsor to prepare a supplement to the IDE for submission to the FDA for review and approval. Once FDA approves the use, the physician must seek concurrence from the IRB Chair to proceed with the use of the device for patient treatment.

3.9.3 **IDE Supplement for FDA Approval and IRB Chair Review**

3.9.3.1 Unlike emergency use of an unapproved device, prior FDA approval is needed before compassionate use occurs. In order to obtain FDA approval, the sponsor should submit an IDE

supplement requesting approval for a protocol deviation under section 812.35(a) in order to treat the patient. The IDE supplement should include the following information, provided by the clinician to the sponsor:

3.9.3.1.1 A description of the patient's condition and the circumstances necessitating treatment;

3.9.3.1.2 A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;

3.9.3.1.3 An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient; and

3.9.3.1.4 The patient protection measures that will be followed. These measures include:

3.9.3.1.4.1 Informed consent from the patient or a legal representative/surrogate;

3.9.3.1.4.2 Clearance from the institution (HHC). Note, in the case of protocols to be carried out at HHC, once approved by the IRB, the physician must bring evidence of IDE approval and accompanying information or protocol to the relevant Vice President or Service Line Director at HHC for approval insofar as inventory and costs may affect Hospital finances and procedures;

3.9.3.1.4.3 Concurrence of the IRB chairperson, based upon the chairperson’s review of the supplemental information prepared for the FDA’s approval, including the patient informed consent form;

3.9.3.1.4.4 An independent assessment from an uninvolved physician; and

3.9.3.1.4.5 Authorization from the IDE sponsor, if an approved IDE exists for the device.

3.9.3.2 The physician should not treat the patient identified in the supplement until FDA approves use of the device under the proposed circumstances. In reviewing this type of request, FDA will consider the above information as well as whether the preliminary evidence of safety and effectiveness justifies such use and whether such use would interfere with the conduct of a clinical trial to support marketing approval. FDA approval should be provided to the IRB Chair for review along with the aforementioned supplemental information.

3.9.4 **Upon FDA clearance, the physician must submit the "Request for Emergency/Compassionate Use of Unapproved Test Article" Form to the IRB office with the supporting documentation described above in order to obtain concurrence of the IRB Chair, or convened IRB if there is sufficient time to review the request prior to the use.**

3.9.5 **Patient Monitoring and Reporting Requirements**

3.9.5.1 If the request is approved by the FDA, and the requisite institutional clearance and IRB Chair concurrence are obtained, the physician should devise an appropriate schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient. The patient should be monitored to detect any possible problems arising from the use of the device. Following the compassionate use of the device, a follow-up report should be submitted to FDA as an IDE supplement in which summary information regarding patient outcome is presented. If any problems occurred as a result of device use, these should be discussed in the supplement and reported to the IRB as soon as possible.

3.9.6 **Compassionate Use for Multiple Patients**

3.9.6.1 The above compassionate use criteria and procedures can also be applied when a physician wishes to treat a few patients rather than an individual patient suffering from a serious disease or condition for which no alternative therapy adequately meets the medical need. In this case, the physician should request access to the investigational device through the IDE sponsor. The sponsor should submit an IDE supplement that includes the information identified above and indicates the number of patients to be treated. Such a supplement should include the protocol to be followed or identify deviations from the approved clinical protocol. As with single patient compassionate use, a monitoring schedule should be designed to meet the needs of the patients while recognizing the investigational nature of the device. Follow-up information on the use of the device should be submitted in an IDE supplement after all compassionate use patients have been treated.

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 21 CFR 50.23, 21 CFR 50.24, and 21 CFR 50.25(d)

5.2 21 CFR 56.102(d) and 21 CFR 56.104(c)

5.3 FDA Device Advice: Investigational Device Exemption (IDE) http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm

5.4 FDA Device Advice: IDE Early/Expanded Access http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionateuse

5.5 FDA IRB Information Sheets – Medical Devices (Updated 9/98) http://www.fda.gov/oc/ohrt/irbs/devices.html#emergency

5.6 FDA, Guidance on IDE Policies and Procedures, January 20, 1998. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm

5.7 FDA, Information Sheet Guidance: Frequently Asked Questions about Medical Devices, January 2006. http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf

5.8 FDA, IRB Information Sheets: Emergency Use of an Investigational Drug or Biologic, September 1998. http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html

5.9 FDA, IRB Information Sheets: Emergency Use of Unapproved Medical Devices, September 1998. http://www.fda.gov/oc/ohrt/irbs/devices.html

6.0 Revision History:

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

Element I.7.C.