1 PURPOSE

1.1 This guidance establishes the process for an investigator conducting planned emergency research with a waiver of consent when more than minimal risk is involved.

1.2 The guidance begins when an investigator is preparing for any planned emergency research or clinical investigation activity that involves human subjects.

1.3 The guidance ends when the planned emergency research is permanently closed with the Sharp HealthCare (SHC) Institutional Review Board (IRB).

2 REVISIONS FROM PREVIOUS VERSION

2.1 If applicable, previous versions are available via the Human Research Protection Program Change Log.

3 POLICY STATEMENT

3.1 The Department of Health and Human Services (DHHS) waiver, just as the Food and Drug Administration (FDA) regulatory change (21 CFR 50.24), provides a narrow exception to the requirement for obtaining and documenting informed consent from each human subject or his or her legally authorized representative (LAR) prior to initiation of research if the waiver of informed consent is approved by an IRB. The ***waiver authorization applies to a limited class of research activities*** involving human subjects who need emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have available a LAR.

3.2 The intent of these regulations is 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 to provide for safe and ethical studies.

3.3 The research plan must be approved in advance by the FDA (when applicable) and the SHC IRB, and publicly disclosed to the community in which the research will be conducted.

3.4 Important Notes:

3.4.1 Planned Emergency Research is not the same as Emergency Use of a Test Article described in *GUIDANCE: Expanded Access Review (HRP-023)*.

3.4.2 In addition, Federal and California State law provides for the conduct of planned research with surrogate informed consent when potential research participants are unable to consent due to decisional impairment. See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013).*

4 RESPONSIBILITIES

4.1 Investigators, IRB members, and IRB Specialists perform these procedures.

5 PROCEDURE

5.1 The SHC IRB reviews and may approve planned emergency research without requiring that informed consent of all subjects be obtained if the SHC IRB (with the concurrence of a licensed physician who is a member of the IRB and is not otherwise participating in the clinical investigation) finds and documents each of the following:

5.1.1 The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of interventions.

5.1.2 Obtaining informed consent is not feasible because:

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

5.1.2.2 The intervention under investigation must be administered before consent from the subjects' LARs is feasible; and

5.1.2.3 There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

5.1.3 Participation in the research holds out the prospect of direct benefit to the subjects because:

5.1.3.1 Subjects are facing life-threatening situation that necessitates intervention.

5.1.3.2 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.

5.1.3.3 Risks associated with the investigation 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.

5.1.4 The clinical investigation could not practicably be carried out without the waiver.

5.1.5 The proposed investigational plan:

5.1.5.1 Defines the length of the potential therapeutic window based on scientific evidence

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

5.1.5.3 The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the same time of continuing review via *FORM: Continuation Request or Final Closure Report (HRP-212)*

5.1.6 The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their LARs in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with information below.

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

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

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

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

5.1.7.4 Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation

5.1.7.5 If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a LAR and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review via *FORM: Continuation Request or Final Closure Report (HRP-212)*.

5.1.7.6 Consenting is an ongoing process. All applicable criteria that would trigger re-consenting a subject in any study also apply to subjects whose consent has been provided by a surrogate. See *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)* for additional information.

5.1.8 In addition to the situations described under section 5.3 of the *GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)*, if the subject is entered into research with waived consent and the subject dies before an LAR or family member can be contacted, information about the research should be provided to the subject's LAR or family member, when feasible.

5.2 Research subject to FDA regulations - The SHC IRB must review and approve both the activity and a waiver of informed consent, and find and document that:

5.2.1 The research activity is subject to regulations codified by the Food and Drug Administration (FDA) (see Federal Register, Vol. 61, pp. 51498-51531) at Title 21 CFR Part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent; and

5.2.2 The requirements for exception from informed consent for emergency research detailed in 21 CFR 50.24 have been met relative to those protocols

5.3 Research subject to International Conference on Harmonisation – Good Clinical Practice (ICH-GCP) (E6) guidelines - The Principal Investigator or designee will inform the subject or the subject's LAR about the clinical trial as soon as possible and will obtain the subject's or LAR's consent if the participant wishes to continue

5.4 Documentation of findings, determinations, and requirements:

5.4.1 The designated IRB reviewer documents their findings via *CHECKLIST: Waiver of Consent Process for Planned Emergency Research (HRP-419)* at the time of initial IRB review and for modifications and continuing reviews where the determinations relevant to this checklist made on the previous review have changed

5.4.2 The IRB Specialists document the SHC IRB's findings, determinations, and requirements via *TEMPLATE: Agenda/Minutes (HRP-501)* when agenda items are reviewed at the convened meeting and *TEMPLATE: Notification of Non-Committee Reviews (HRP-501b)* when agenda items are reviewed via expedited procedures (when allowed by the regulations)

6 MATERIALS

6.1 GUIDANCE: Legally Authorized Representatives (Surrogate Consent) (HRP-013)
6.2 GUIDANCE: Expanded Access Review (HRP-023)
6.3 FORM: Continuation Request or Final Closure Report (HRP-212)
6.4 CHECKLIST: Waiver of Consent Process for Planned Emergency Research (HRP-419)
6.5 TEMPLATE: Agenda/Minutes (HRP-501)
6.6 TEMPLATE: Notification of Non-Committee Reviews (HRP-501b)

7 REFERENCES

7.1 FDA: 21 CFR 50.24; FDA Guidance - Exception from Informed Consent Requirements for Studies Emergency Research
7.2 DHHS: 45 CFR 46.116(f); DHHS Guidance - Informed Consent Requirements in Emergency Research (OPRR Letter, 1996)
7.3 ICH-GCP (E6): 3.1.7; 4.8.15

This document is available on IRBANA or by contacting research@sharp.com.