SAINT AGNES MEDICAL CENTER
CLINICAL RESEARCH CENTER
Fresno, California

Standard Operating Procedures
Institutional Review Board

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SUBJECT: HUMANITARIAN USE DEVICES

I. PURPOSE

Outline the requirements and procedure for the submission of a proposal to use a humanitarian use device (HUD) on human subjects.

2. SCOPE

This applies to any use of an HUD within Saint Agnes Medical Center facilities or an Investigator's office/clinic.

3. POLICY

All intended uses of an HUD must be reviewed and approved by the Institutional Review Board (IRB) before being used with the exception of emergency use.

4. PROCEDURE

4.1 KEY DEFINITIONS:

Humanitarian Use Device (HUD): a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. Use of an HUD is not research but rather is use of a legally marketed device.

Humanitarian Device Exemption (HDE): is an application to the FDA that is similar to a premarket approval (PMA) application but is exempt from the effectiveness requirements of sections 514 and 515 of the Food Drug and Cosmetic Act. FDA approval of and HDE authorizes an applicant (the HDE holder) to market the HUD

subject to certain profit and use restrictions. HUDs can not be sold for profit, except in narrowly defined circumstances, and they can only be used in a facility after an IRB has approved their use in that facility, except in certain emergencies.

4.2 HUD IRB SUBMISSION:

The Investigator must submit a "Humanitarian Use Device Application" to the IRB for review and approval by the due date published by the IRB Administrator. The Investigator **can not** initiate use of the HUD without IRB approval unless for emergency situations (see section 4.3 below).

To be considered for review, each Investigator must submit and sign a 'Humanitarian Use Device Application' accompanied by the following required documents:

- a copy of the FDA's HDE approval letter;
- the current version of the HUD protocol if available, or at least a summary of its intended use, applicable patient population and a description of the tests, procedures and evaluations the Investigator will perform;
- a copy of the current product labeling;
- a description of the device (e.g., the current version of the Investigator's Brochure (IB) or device brochure);
- if requested by the IRB, a proposed patient Informed Consent drafted using the SAMC IRB Informed Consent template, specifically if the HUD is being studied in a clinical investigation, the informed consent of the patient must be obtained;
- any patient information packet to be given to prospective patients describing potential risks **and that the device's effectiveness has not been demonstrated**;
- a signed 'Statement of the Investigator';
- an Investigator-signed financial disclosure;
- Investigator(s) curriculum vitae and medical license;
- Confirmation that the Investigator has completed recent training in human subjects research offered through Collaborative Institutional Training Initiative (CITI) or National Institutes of Health (NIH).

4.2 IRB REVIEW AND CRITERIA FOR APPROVAL

Even though use of a HUD for its approved indication is not considered research, the criteria for IRB approval, *in general,* are essentially the same as those stated in IRB SOP R-1209, specifically:

- risks to subjects are reasonable in relation to any possible anticipated benefits knowing that the effectiveness of the HUD has not been demonstrated;
- selection of subjects is equitable within the FDA-approved use of the HUD;

- informed consent is generally not be required unless the HUD is being studied in a "clinical investigation" (i.e., collecting safety and/or effectiveness data for its approved indication, or collecting safety and efficacy data under an FDA-approved IDE). In these investigational situations, reasonable safeguards must be included in order to protect the rights and the welfare of vulnerable populations (e.g., children, pregnant women) and those patients likely to be vulnerable to coercion or undue influence (e.g., decisionally-compromised individuals or individuals whose cultural predisposition is to not question a doctor's recommendation/authority);
- HIPAA authorization is generally not required unless use of the HUD is in the context of a clinical investigation. Even so, the IRB or Privacy Board may at its discretion choose to waive the HIPAA authorization because the research satisfies certain waiver criteria [IRB SOP R-1230]. Reporting safety information to the Sponsor does not require a HIPAA authorization since it falls under the permissive disclosure for FDA-related activities at 45 CFR 164.512(b)iii.

Use of an HUD will be subject to initial full-board review and continuing review by the IRB. The IRB may use its discretion to determine how to approve the HUD, for example: it may solicit input from appropriate expertise external to the IRB, it may specify limitations on the use of the device based on one or more measures of disease progression, it may require appropriate follow-up precautions and evaluations, etc. For continuing review, the IRB may use expedited review procedures unless it decides that full-board review is necessary.

4.3 HUD USE IN EMERGENCY AND COMPASSIONATE USE

A. Emergency Use:

In an emergency situation, a HUD may be used off-label (i.e., outside its approved indication for use) to save the life or protect the physical well-being of a patient from serious harm, however the treating physician should try to obtain the following whenever possible:

- the IRB Chairperson's concurrence if possible;
- the informed consent of the patient or his/her legal representative;
- an independent assessment by an uninvolved physician (i.e., not the referring);
- institutional clearance
- authorization from the HDE holder

Additionally, the physician must report the emergency use within five (5) days; provide written notification to the IRB Chairperson, including identification of the patient involved, the date of use, and the reason for the use.

B. Compassionate Use:

A physician who wants to use a HDE-approved device for compassionate use should provide the HDE holder and the IRB with:

- a description of the patient's condition;
- the circumstances necessitating use of the device;
- a discussion of why alternative therapies or diagnostics are unsatisfactory;
- information to address the patient protection measures

4.4 Physician or Investigator Reporting Responsibilities

A. Safety Reporting:

As HUD's are legally marketed devices being used for an approved indication, whenever an HUD may have reasonably caused or contributed to a death or serious injury, or has malfunctioned and would likely cause or contribute to a death or serious injury if the malfunction were to recur, the user facility (i.e., Saint Agnes or Investigator's clinic/office) must submit a Medical Device Report (MDR) to the IRB of record, the FDA and the manufacturer. The specific requirements for MDR reporting are set forth in 21 CFR 803.

Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a body function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or structure.

Permanent means irreversible impairment or damage to a body structure ro function, excluding trivial impairment or damage.

For Investigational use of a HUD under an IDE, reports of Unanticipated Adverse Device Effects must be reported under 21 CFR 812.150(a)(1) and 812.150(b)(1).

An Unanticipated Adverse Device Effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

B. Study Status Reporting:

The physician must provide the IRB with periodic updates as to the use of the HUD. This may be annually or more frequent as determined by the IRB. When the physician no longer wishes to use the HUD, the physician will provide the IRB with a 'Final Report' delineating the number of patients on whom the HUD was used (for diagnosis or treatment) and an accounting of all deaths and life-threatening events that may have reasonably been caused by the device and whether or not such suspect events were reported to the facility, FDA, IRB and device manufacturer.

REGULATORY REFERENCES

21 CFR 803	Medical Device Reporting
21 CFR 814.100	Humanitarian Use Devices
FDA Guidance	Guidance for HDE Holders, IRBs, Clinical Investigators, and FDA Staff (July 8, 2010)
FDA Guidance	Humanitarian Device Exemption (HDE) Regulation: Q & A, July 18, 2006