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IRB Help Sheet

Humanitarian Use Devices (HUDs)
Humanitarian Device Exceptions (HDEs)

Introduction

Humanitarian Use Devices (HUDs) are devices that are intended to benefit patients in the treatment and diagnosis of disease or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year [21 CFR 814, Subpart H]. Device manufacturers must seek a Humanitarian Device Exemption in order to market such devices. A Humanitarian Device Exemption (HDE) is an application that is similar to a premarket approval (PMA) application; however it is exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD). The FDA mandates that an IRB must oversee the use of humanitarian use devices even in purely treatment settings. The statute and the implementing regulation (see 21 CFR 814.124(a)) require IRB review and approval before a HUD is used. This policy applies to physicians intending to treat patients at OHSU with a HUD.

This Help Sheet is a supplement to:

- POLICY HRP-080: IRB Member Review Expectations HUD
- WORKSHEET HRP-450: Criteria for Approval HDE Use

Click on a link below to jump to that section:

1. General Guidelines

A. Initial and continuing review by the OHSU IRB is required for the use of HUDs even if there is no intent to collect data.

B. Use of a HUD within its approved labeling does not constitute research by the Common Rule definition.

C. All proposed uses of HUDs at OHSU must be reviewed by the OHSU IRB at a convened meeting of the full board prior to any provision of patient care or treatment with the HUD. There is an exception to this rule in emergency situations.

D. Continuing review will be on an annual basis using expedited review procedures as long as use of the HUD within its approved labeling. The regulations do allow the IRB to require shorter

reviews intervals or full board review at each review and the IRB will only do so in exceptional cases.

E. Clinical Investigation of a HUD beyond its FDA approved indication requires an approved Investigational Device Exemption (IDE) and the OHSU IRB will not approve it otherwise.

F. An HDE holder may collect safety and effectiveness data to support a PMA for the HDE-approved indication without an IDE. However, compliance with 21 CFR part 50 is required.

G. The IRB will require prospective informed consent unless it determines that obtaining consent is impracticable. The informed consent document must be reviewed and approved by the IRB.

H. The PI is required to submit a report to the FDA whenever:

- **i.** A device with an approved HDE may have caused or contributed to a death or serious injury; or
- **ii.** A device has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

I. As provided by 21 CFR 814.82(a)(9), in order to provide continued reasonable assurance of the safety and probable benefit of the device, the holder shall submit adverse reaction or device defect reports to the IRB.

J. The IRB does not require review and approval of each individual use of a HUD, as long as each use of the HUD is within the FDA approved indication and has been approved by the IRB. The regulations do allow the IRB to restrict its approval; therefore the IRB may approve use of the HUD without any further restrictions, use of the device under a protocol, or use of the device on a case-by-case basis.

2. <u>Sponsor's Responsibilities (including Investigator Sponsor)</u>

A. In accordance with 21 CFR 814.102(a), your request to the FDA for HUD designation must include:

- **i.** a statement indicating you are requesting a HUD designation; the name and address of the applicant;
- **ii.** a description of the disease or condition for which the device is intended;
- **iii.** a description of the device;
- **iv.** documentation, with appended authoritative references, to demonstrate that the device meets the definition of 21 CFR 814.3(n).
- **v.** the name and address of the applicant;
- **vi.** a description of the disease or condition for which the device is intended;
- **vii.** a description of the device;
- **viii.** documentation, with appended authoritative references, to demonstrate that the device meets the definition of 21 CFR 814.3(n).

B. Submit your request for a HUD designation before submitting an application for an HDE

C. When submitting an application for an HDE, include the FDA's HUD designation letter in your application.

D. The HDE application must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use.

E. By statute, approval of an HDE is valid for a period of 18 months, after which the device may no longer be marketed unless the HDE holder has sought and obtained an extension as provided for in Section 814.120 of subpart H Requests must be submitted at least 90 days prior to the expiration of marketing approval.

3. Principal Investigator's (PI) Responsibilities

A. The PI is responsible for obtaining IRB approval before the HUD is administered to or implanted into a patient.

B. To obtain IRB approval, the physician must submit the following materials to the IRB:

- **i.** The HUD manufacturer's product labeling, clinical brochure, and other pertinent manufacturer information materials;
- **ii.** The FDA HDE approval letter.
- **iii.** A HUD protocol including a statement specifying the clinical indication, where and by whom the HUD will be used within the OHSU environment;
- **iv.** A treatment consent form that addresses the proposed clinical use of the HUD. Since the HUD is approved for clinical use by the FDA, words such as 'research" or "study" should be avoided in this clinical consent form.
  - **a.** Physicians may use the HUD consent form template or request IRB approval of an alternate consent form.
  - **b.** The informed consent may be the use or modification of the patient labeling information, if available. Most HDE holders develop patient labeling that incorporates information to assist a patient in making an informed decision about the use of the device. Usually, the patient labeling contains a discussion of the potential risks and benefits of the device as well as any procedures associated with the use of the HUD. It also states that the device is a humanitarian use device for which effectiveness for the labeled indication has not been demonstrated.

C. IRB approval is required for any modifications of the device and/or proposed clinical use of the device.

D. Renewal of IRB approval is secured via the continuing review process. For continuing review, submit the following information:

- **i.** A copy of the current FDA-approved product labeling for the HUD.
- **ii.** For each patient whom the HUD has been used during the previous year provide a summary of:
  - **a.** The clinical indication for the use of the HUD;
  - **b.** Any adverse events felt to be related or possibly related to the use of the HUD; and
  - **c.** The clinical outcomes of the use of the HUD

E. The PI must only use the device within the scope of its labeling.

F. All devices must be kept secure and only used by physician's approved by the IRB.

4. IRB's Responsibilities

A. Adverse Reaction and Device Defect Reporting

- **i.** Per 21 CFR 803, the physician/investigator will be required to report device-related deaths and serious injuries (if the device manufacturer is unknown).
- **ii.** Such reports should be submitted within 10 days after the HDE holder receives or has knowledge of information concerning:
  - **a.** A mix-up of the device or its labeling with another article;
  - **b.** Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and has not been addressed by the device's labeling or has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

c. Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved HDE that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling.

iii. The report shall include:

a. a discussion of the HDE holder's assessment of the change, deterioration, or failure; and

b. any proposed or implemented corrective action by the firm.

B. Off-Label Use of a HUD in Emergency or Compassionate Situations

i. It is recognized that there may be circumstances in which "off-label" use of a HUD may be necessary to save the life or protect the well-being of a patient.

ii. When this situation arises, the physician-investigator should determine if the situation meets the requirements for emergency use of the device. See "WORKSHEET HRP-452: Emergency Use Devices."

iii. If circumstances do not qualify for emergency use, but the physician determines that there is no other alternative device for the patient's condition, a HUD may be used for compassionate use. However, prior FDA and IRB approval is needed before compassionate use occurs to help ensure adequate patient protection. See "WORKSHEET HRP-453: Compassionate Use Devices."

C. Informed Consent

i. The IRB requires treatment consent unless it determines that obtaining consent is impracticable.

ii. The informed consent may be the use or modification of the patient labeling information, if available. Most HDE holders develop patient labeling that incorporates information to assist a patient in making an informed decision about the use of the device. Usually, the patient labeling contains a discussion of the potential risks and benefits of the device as well as any procedures associated with the use of the HUD. It also states that the device is a humanitarian use device for which effectiveness for the labeled indication has not been demonstrated.

D. IRB Review

i. Initial and continuing review by the OHSU IRB is required for the use of HUDs even if there is no intent to collect data.

ii. All proposed uses of HUDs at OHSU must be reviewed by the OHSU IRB at a convened meeting of the full board prior to any provision of patient care or treatment with the HUD.

iii. Continuing review will be on an annual basis. The IRB will use the expedited continuing review procedures at its discretion.

iv. The IRB does not require review and approval of each individual use of a HUD, as long as each use of the HUD is within the FDA approved indication and has been approved by the IRB. However, the regulations do allow the IRB to restrict its approval.