


|  |  |                       |
|--|--|-----------------------|
|  <b>Research Integrity Office</b> | <b>Human Research Protection Program<br/>Policies &amp; Procedures</b> |                       |
| <b>Title: Humanitarian Use Device (HUD)<br/>Humanitarian Device Exemption (HDE)</b>                                | Date Effective<br>4/21/2008  | Supersedes P&P dated: |
|  | Identification   | Page 1 of 4           |

## Background

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 per year in the United States [21 CFR 814, Subpart H]. Device manufacturers must seek a Humanitarian Device Exemption (HDE) in order to market such devices. A HDE is an application that is similar to a premarket approval application (PMA); however, it is exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a HUD. The FDA mandates that an IRB must oversee the use of HUDs 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. A brief summary of the FDA regulations and guidance concerning HUDs can be found at the following website:  
<http://www.fda.gov/cdrh/ode/guidance/1381.pdf>

## Scope

This policy applies to providers intending to treat patients at OHSU with an HUD.

## Authority

Federal Drug Administration <http://www.fda.gov/cdrh/ode/hdeinfo.html>  
 FDA Humanitarian Device Exemptions; Final Guidance <http://www.fda.gov/cdrh/ode/guidance/1381.pdf>  
 21 CFR 814 Subpart H, Humanitarian Use Devices

## I. Policy

- 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. See policy.
- D. Continuing review will be on an annual basis using expedited review procedures as long as use of the HUD within its approved labeling continues. The regulations do allow the IRB to require shorter reviews intervals or full board review at each review and the IRB will do so at its discretion.
- E. Clinical Investigation of a HUD beyond its FDA approved indication requires an approved Investigational Device Exemption (IDE) and the OHSU IRB cannot 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. Informed Consent
  - i. The IRB will require prospective informed consent unless it determines that obtaining consent is impracticable.
  - ii. The informed consent document must be reviewed and approved by the IRB.
- H. Reporting Requirements

- i. Under 21 CFR Part 803 the PI is required to submit a report to the FDA whenever:
  - a. A device with an approved HDE may have caused or contributed to a death or serious injury; or
  - b. 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.

## II. Procedure

### A. Sponsor's Responsibility (including Investigator Sponsor)

- i. In accordance with 21 CFR 814.102(a), a request to the FDA for HUD designation must include:
  - a. a statement indicating who is requesting an HUD designation;
  - b. a description of the disease or condition for which the device is intended;
  - c. a description of the device;
  - d. documentation, with appended authoritative references, to demonstrate that the device meets the definition of 21 CFR 814.3(n).
- ii. Submit requests for an HUD designation before submitting an application for an HDE
- iii. When submitting an application for an HDE, include the FDA's HUD designation letter in the application.
- iv. 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.
- v. 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.
- vi. If an HDE application is not approved, the applicant may appeal the FDA's decision. There is a specific appeal process that must be followed. Please see the FDA's website <http://www.fda.gov/cdrh/modact/dispresl.pdf>

### B. The Principal Investigator's (PI) Responsibility

- i. The PI is responsible for obtaining IRB approval before the HUD is administered to or implanted into a patient.
- ii. To obtain IRB approval, the provider must submit the following materials to the IRB:
  - a. The HUD manufacturer's product labeling, clinical brochure, and other pertinent manufacturer information materials;
  - b. The FDA HDE approval letter.
  - c. A HUD protocol including a statement specifying the clinical indication(s) and where and by whom the HUD will be used within the OHSU environment; and
  - d. 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.
    - Providers may use the HUD consent form template or request IRB approval of an alternate consent form.
    - Information in the informed consent form may use or modify 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.

- iii. IRB approval is required for any modifications of the device and/or proposed clinical use of the device.
- iv. Renewal of IRB approval is secured via the continuing review process. For continuing review, submit the following information:
  - a. A copy of the current FDA-approved product labeling for the HUD.
  - b. For each patient for whom the HUD has been used during the previous year provide a summary of:
    - The clinical indication for the use of the HUD;
    - Any adverse events felt to be related or possibly related to the use of the HUD; and
    - The clinical outcomes of the use of the HUD
- v. The PI must only use the device within the scope of its labeling.
- vi. All devices must be kept secure and only used by providers approved by the IRB.

**C. IRB's Responsibility**

**i. Adverse Reaction and Device Defect Reporting**

- a. Per 21 CFR 803, the provider/investigator will be required to report device-related deaths and serious injuries (if the device manufacturer is unknown).
- b. Such reports should be submitted within 10 days after the HDE holder receives or has knowledge of information concerning:
  - A mix-up of the device or its labeling with another article;
  - 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.
  - 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.
- c. The report shall include:
  - a discussion of the HDE holder's assessment of the change, deterioration, or failure; and
  - any proposed or implemented corrective action by the firm.

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

- a. 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.
- b. When this situation arises, the provider/investigator should determine whether the situation meets the requirements for emergency use of the device, see "Emergency Use of an Investigational Drug, Device, or Biologic" policy.
- c. If circumstances do not qualify for emergency use, but the provider 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.
- d. A provider who wishes to use a HDE-approved device for compassionate use should provide the HDE holder 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; and
  - information to address the patient protection measures.

**iii. Informed Consent**

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

- b. Information in the informed consent form may use or modify the patient labeling information, if available.

iv. IRB Review

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

III. **Definitions**

- A. A **Comparable Device** need not be identical to the device submitted under an HDE application. In determining whether a comparable device exists, FDA will consider:
  - The device's intended use and technological characteristics;
  - The patient population to be treated or diagnosed with the device; and
  - Whether the device meets the needs of the identified patient population.
- B. **Compassionate Use** - Circumstance in which the only option available for a patient faced with a serious, albeit not life-threatening condition, is use of the device.
- C. **Emergency Use** – Circumstance in which IRB approval cannot be obtained in time to prevent serious harm or death to the patient.
- D. **A Humanitarian Device Exemption (HDE)** - is an application that is similar to a pre-market approval (PMA) application, but exempt from the effectiveness requirements of sections 514 and 515 of the act. FDA approval of an HDE authorizes marketing of an HUD.
- E. **Humanitarian Use Devices (HUDs)** – 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.
- F. **Premarket Approval (PMA) Application** – An approved Premarket Approval Application (PMA) is FDA permission to the applicant for marketing a particular medical device. Premarket approval by FDA is the required process of scientific review to ensure the safety and effectiveness of Class III devices.
- G. **Unapproved medical device** – a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e)(the act) or an approved IDE under section 520(g) of the act (21 U.S.C. 360j(g)).