SPECTRUM HEALTH
Human Research Protection Program
Office of the Institutional Review Board
100 Michigan NE, MC 038
Grand Rapids, MI 49503
616.486.2031
irb@spectrumhealth.org
www.spectrumhealth.org/HRPP

Humanitarian Use Devices: Frequently Asked Questions

A Spectrum Health IRB Guidance Document

Purpose

This document provides guidance on many common questions the IRB receives related a Humanitarian Use Device (HUD). The questions and answers provided in this guidance are from the FDA Guidance entitled "Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff: Humanitarian Device Exemption (HDE) Regulation: Question and Answers July 8, 2010". Contact the IRB office at (616) 486-2031 or irbassist@spectrumhealth.org if you have additional questions or need assistance regarding HUDs.

FAQs

1. *What is a Humanitarian Use Device (HUD)?*
   As defined in 21 CFR 814.3(n), a HUD is 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."

2. *Is a HUD approved by the FDA?*
   Yes. To obtain approval for an HUD, a humanitarian device exemption (HDE) application is submitted to FDA. An HDE is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for 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, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market. An approved HDE authorizes marketing of the HUD.

3. *Does using a HUD constitute human subject research?*
   No. Using a HUD per the FDA Approved Use/Label does not constitute human subject research. However, a confusing aspect for HUD use if the FDA regulations require that a HUD may only be used in facilities that have established a local institutional review board (IRB) to supervise clinical testing of devices and after an IRB has approved the use of the device to treat or diagnose the specific disease. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.

4. *Are there unique storage requirements for HUDs?*
   Yes. Steps should be taken by the healthcare provider overseeing the use of the HUD at the institution to ensure the HUD is properly labeled, tracked, and used in a manner approved by the FDA, IRB, and device manufacturer. The IRB must be provided information on the number of HUDs used during the course of a year at the institution.

5. *Does a HUD require initial and continuing review by the IRB?*
   Yes. As stated in section 529(m)(4) of the Federal Food, Drug, and Cosmetic Act (the Act), IRB approval is required before a HUD is used at a facility, with the exception of emergency use. The IRB will verify amongst other items, the qualifications of the healthcare provider planning to use the HUD, the plans to inform patients of the lack of effectiveness data, and plans for ensuring proper use of the device at the institution. The IRB will also verify the healthcare provider intends to use the device per approved indication. Using a HUD off-label, may constitute a clinical investigation subject to IDE and human subject research regulations. For continuing review, the IRB must review the HUD activities at least once a year, but may use the expedited review process unless concerns occurred over the year that warrants a review by the full board.

6. *If there is an adverse event in a HUD patient, do I need to submit an RNI to the IRB?*
   Yes, if it meets the IRB reporting requirements. The requirements to be reported are the event must be unexpected, at least probably related and places a greater risk of harm than was previously known or recognized. Device user facilities and manufacturers are required to submit medical device reports to FDA and to the "IRB of record" (i.e., the IRB approving the use of the HUD). Among these requirements, manufacturers must submit reports to FDA and the IRB of record whenever a HUD may have caused or contributed to a death or serious injury, or has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur. User facilities must submit reports to FDA, the IRB of record, and the manufacturer whenever a HUD may have caused or

contributed to a death, and must submit reports to the manufacturer (or to FDA and the IRB of record if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)). 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 permanent damage to a body structure (21 CFR 803.3).

7. *Is an IRB approved informed consent form required for HUD patients?*
   No. Furthermore, neither the Act nor the regulations require informed consent from patients for the use of a HUD.

   However, the IRB may choose to require informed consent that is consistent with the approved labeling when the IRB approves use of the HUD in a facility. Most HDE holders develop patient information packets that generally contain a discussion of the potential risks and benefits of the HUD and any procedures associated with its use. If patient information packets are available, the IRB should ensure that physicians distribute them to patients prior to their receiving the HUD. Even when an institution requires patients to sign a written consent document that describes the use of the HUD (and which may provide similar information found in the HDE holder's packet), the patient should always receive the HDE holder's patient information packet. For HUD patient information packets, go to http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm#2 and select the HDE number. In addition to the above information, many institutions also require informed consent for the surgery or procedure related to the use of the HUD.

   If a HUD is studied in a clinical investigation, the informed consent of the subject must be obtained in accordance with FDA human subject research regulations at 21 CFR Part 50.

8. *Can a HUD be used off-label in a compassionate or emergency use situation without prior IRB approval?*
   Yes. However, physicians should be cognizant that FDA has made a determination of safety and probable benefit for use of the HUD only within its approved indication(s). If a physician wants to use a HUD outside its approved indication(s), the FDA recommends that the physician obtain informed consent from the patient and ensure that reasonable patient protection measures are followed, such as devising schedules to monitor the patient, taking into consideration the patient's specific needs and the limited information available about the risks and benefits of the device. FDA further recommends that the physician submit a follow-up report on the patient's condition to the HDE holder and first check with the IRB before such compassionate use to review any institutional policy.

   In addition, if the physician in an immediate emergency use situation and determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. However, the physician must report the emergency use within five days in writing regarding the use to the IRB Chairperson including identification of the patient involved, the date of the use, and the reason for the use per section 520(m)(4) of the Act; 21 CFR 814.124.

9. *What are the differences between a HUD use, Emergency Use HUD, Compassionate Use HUD, and Investigational Use HUD?*
   - It is recommended you review the FDA Guidance entitled "Guidance on IDE Policies and Procedures January 20, 1998" and "Guidance for HDE Holders, Institutional Review Boards

(IRBs), Clinical Investigators, and Food and Drug Administration Staff: Humanitarian Device Exemption (HDE) Regulation: Question and Answers July 8, 2010" to further understand the regulatory differences. However, here is a brief summary of the differences:

- **Humanitarian Use Device use:** Use per FDA approval label at institution with IRB approval. Can be used several patients a year. Consent [to treat] is required per IRB requirements.

- **Emergency Use HUD:** Use per FDA approval prior securing IRB approval at the institution **OR** use off-label of the HUD in an immediate life-threatening situation where no alternative effective treatment exist. Single subject situation requires IRB notification within 5 days of occurrence. Consent [to treat] is not required if true emergency situation. However, attempts should be made to secure consent from family member/legally authorized representative (LAR) if possible prior use. As the subject medical conditions improves both subject and family member/LAR (if applicable) should be informed of what happened as soon as feasible.

- **Compassionate Use HUD**: Use off-label of a HUD in a (non-urgent) life-threatening situation where no alternative effective treatment exists. Single patient situation that requires IRB approval prior use. Consent [to treat] is required per IRB requirements.

- **Investigation Use HUD:** An off-label use being studied under a research study in compliance with IDE regulations 21 CFR Part 812. Requires IRB approval prior use. Can be used in several subjects per year. Use of IRB approved Research Informed Consent is required.