Marshfield Clinic

Humanitarian Use Devices

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Humanitarian Use Device (HUD)

- A medical device that is designed to treat or diagnose an "orphan disease" (i.e., a disease or condition that affects, or is manifested in, fewer than 4,000 individuals in the U.S. per year). In the case of a device used for diagnostic purposes, documentation must demonstrate that fewer than 4,000 individuals per year would be subject to diagnosis by the device in the U.S.

2.2. Humanitarian Device Exemption (HDE)

- An application to the FDA seeking exemption from the effectiveness requirements of sections 514 and 515 of the Federal Food, Drug and Cosmetic Act. This application is filed after the FDA determines the device qualifies as a HUD. FDA approval of an HDE authorizes an applicant to market the HUD, subject to certain profit and use restrictions.
- An HDE must contain sufficient information for the FDA to determine, among other things, whether or not the HUD poses an unreasonable or significant risk of illness or injury, and whether the anticipated benefit from its use outweighs associated potential risks of injury or illness, taking into account known risks and benefits of currently available devices or alternate forms of treatment. The HDE applicant must also demonstrate that no comparable FDA-approved devices are available to treat or diagnose the disease or condition, and that the device could not otherwise be brought to market without HUD status.

2.3. Use of a HUD

- Clinical deployment of a HUD according to its approved labeling and indication(s) to treat or diagnose patients (not research).

2.4. Investigational Use / Clinical Investigation of a HUD

- Collection of safety and effectiveness data on the HUD while it is in use (research).

3. PROCEDURE BODY

This document outlines the requirements for use of Humanitarian Use Devices (HUDs) at Marshfield Clinic and all institutions for which MCRF serves as IRB of record, as well as the requirements for investigational use / clinical investigation of HUDs.

3.1. Obtaining an Approved HDE

a. In order to obtain FDA approval for HUD use through an HDE, an applicant must contact the FDA Office of Orphan Products Development, which is responsible

Live
PROCEDURE

for determining whether the device qualifies as a HUD. 21 CFR 814.102(a) outlines the information needed by the FDA to make the determination.

b. Once the FDA determines that the device is a HUD, the applicant must then submit a Humanitarian Device Exemption (HDE) application to the FDA, including a reference to the FDA's earlier determination.

c. The FDA's approval of the HDE will include the approved indication(s). A new application must be submitted for any additional indications desired by either filing a separate HDE or IDE, as described below.

3.2. Uses and Review Requirements of a HUD

a. HUD Use For Approved Indication With No Collection of Safety and Effectiveness Data ("Clinical Use")

- An approved HDE authorizes the marketing of a HUD for clinical use (i.e., treatment or diagnosis) within the scope of the HDE-approved indication, and as authorized by the local IRB.
- IRB Review
  - Use of a HUD for clinical treatment and/or diagnosis of a condition without concurrent collection of safety or effectiveness data is not considered human subjects research. However, the FDA still requires an IRB to initially review and approve local HUD use, as well as conduct continuing reviews.
  - Any physician or other staff planning to use a HUD for a clinically approved indication, but with no plans to collect safety and effectiveness data, must obtain prior IRB review and approval of HUD use.
  - The form "IRB Application - Humanitarian Use Device (HUD)" should be completed and submitted to ORIP to initiate IRB review.
  - The IRB may request and review the following materials during initial review of the HUD:

    A copy of the HDE approval order;

    A description of the device;

    The product labeling;

    The patient information packet that may accompany the HUD;

    If appropriate, a sample consent form authorizing use of the HUD; and

    A summary of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests, or procedures.
  - The convened MCRF IRB will conduct the initial review.
  - MCRF IRB will consider potential risks to patients, whether the risks are minimized, and whether the risks are reasonable in relation to the

Live
PROCEDURE

proposed use of the HUD. MCRF IRB will also consider the training and expertise of physicians applying to use the device.

- For each HUD approved, the IRB will:

  Specify approval for HUD use in an individual patient or a specific number/group of patients, and may place limits based on measures of disease progression, prior use and failure of alternative treatment requirements, or appropriate follow-up precautions and evaluations;

  Determine what information about the HUD, if any, must be given to patients in addition to the patient information brochure; and

  Specify the timeframe for continuing review.

- Continuing review may be conducted via expedited review. Continuing use of an HUD will be reviewed at least annually, and more frequently if warranted by anticipated risks. See "Determining Which Projects Require Review More Often than Annually." The form "IRB Continuation Request" must be completed and submitted to ORIP at time of continuing review.

 Informed Consent

- While not required by FDA regulations (21 CFR 814, Subpart H), the IRB may require informed consent to be obtained. At a minimum, the MCRF IRB typically requires that the manufacturer's patient information brochure, or other information about the HUD, be provided to patients.

 HIPAA Authorization

- Since the HUD is not being used in a clinical investigation (research), the Protected Health Information may be used or disclosed for treatment or diagnostic purposes without the patient's authorization.

 Restrictions on Location of HUD Use

- A HUD may only be used by IRB approved physicians in facilities designated by the IRB overseeing use of the HUD.

 Labeling

- HUD labeling must indicate that the device is a HUD, and that although its use has been authorized for clinical use by federal law, its effectiveness for the specific clinical indication for which it has been approved has not been demonstrated.

b. HUD Use With Collection of Safety and Effectiveness Data – Approved or Unapproved Use ("Clinical Investigation," Research)

 IRB Review

- When the HDE holder or user collects safety and effectiveness data on the use of the HUD, the use is considered a "clinical investigation," and thus, human subjects research. All requirements for reviewing and conducting human subjects research, and all IRB policies and procedures, will apply.

When document is printed it becomes an uncontrolled copy. Please refer to DCS system for most current version.

PROCEDURE

- The form "IRB Application – New Research" should be completed and submitted to ORIP to initiate IRB review.
- In addition to the standard information requested at initial review for any clinical investigation, the IRB may request the following materials during initial review of the HUD:

  A copy of the HDE approval order;

  A description of the device;

  The product labeling;

  The patient information packet that may accompany the HUD;

  If appropriate, a sample consent form authorizing use of the HUD; and

  A summary of how the physician proposes to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests, or procedures.
- The IRB will make a Significant Risk/Non-Significant Risk (SR/NSR) determination only when the clinical investigation is for an indication different than the HDE-approved indicator.

- If the HUD use is for an approved indication, an Investigational Device Exemption (IDE) is not required even if the HDE holder plans to use the data collected to support a pre-market approval application. An IDE is required, however, for clinical investigations involving unapproved uses.

c. Emergency Use of HUDs

- The FDA permits "emergency use" of HUDs in treating unique patients for whom no effective alternative treatment exists.
- For a HUD to be used on an emergent basis, there must be insufficient time to obtain IRB approval prior to its use. The physician or staff person must first contact the Office of Research Integrity & Protections to determine whether a meeting of the convened Marshfield Clinic Research Foundation IRB (MCRF IRB) can take place before the anticipated use of the HUD.
- If prior IRB approval is not feasible, the physician must report the emergency use to the IRB Chairperson within five working days. This written report must include notification of the use, identification of the patient involved, the date of the use, and the reason for the use.
- A research informed consent need not be obtained prior to emergency use of the HUD. The IRB may require the product information sheet or other information be given to the patient.

3.3. Additional Reporting Requirements

a. A HUD manufacturer must submit required reports to the FDA and the IRB, and facilities using the HUD must submit reports to the FDA, overseeing IRB, and manufacturer, whenever:

Live
PROCEDURE

- The HUD may have caused or contributed to a death or serious injury, or has been found to have malfunctioned would be likely to cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 803.50 and 814.126(a); 21 CFR 803.30 and 814.126(a)). Serious injury means an injury that is:
  - Life-threatening;
  - Results in permanent impairment of a body function or permanent damage to a body structure; or
  - Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
- Such events must be reported to ORIP within **10 days** of any individual involved in the HUD use becoming aware of the incident.

The HDE holder is responsible for making all necessary periodic reports as required in the HDE approval order.

4. ADDITIONAL RESOURCES

4.1. IRB Form for submission

- IRB Application – Humanitarian Use Device
- IRB Application – New Research
- IRB Continuation Request
- IRB Change or Update to Original Submission
- IRB ICH GCP Adverse Event Report
- IRB Unanticipated Problem Report

4.2. References:

- Determining Which Projects Require Review More Often than Annually
- Expanded Access to Investigational Drugs, Biologics or Devices (Individual Patient, including Emergency Use, Intermediate Size Populations, Treatment)
- Human Participants in Research
- Informed Consent
- IRB Review of Investigational Device Research

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control transferred from Policy & Handbook Library - #805.3 (no changes made)
2.0	Add hyperlink to applicable IRB forms and referenced policies

Live
PROCEDURE

6. DOCUMENT PROPERTIES

Primary Author: Scheller, Lori A
Co-Author(s):
Approver(s): This document has been electronically signed and approved by: Ziemba, Steven J PHD on: 12/1/2015 4:13:18 PM

Live

PROCEDURE