

Appendix N

Humanitarian Device Exemption (HDE) Requirements

On June 26, 1996, the FDA issued a final rule (21 CFR Part 814) to carry out the provisions of the Safe Medical Devices Act of 1990 regarding humanitarian use devices (HUDs). A HUD is a device that is intended for the diagnosis or treatment of a disease or condition that affects fewer than 4,000 individuals in the United States per year. Since a device manufacturer's research and development costs could exceed its market return for diseases or conditions affecting such small patient populations, the FDA promulgated this regulation to provide an incentive for the development of devices for such humanitarian use.

The regulation provides for the FDA submission of a humanitarian device exemption (HDE) application, which is similar in both form and content to a premarket approval (PMA) application. However, unlike a PMA application, 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 HDE application must, however, 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; taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the HDE applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that the device could not otherwise be brought to market unless it is granted HUD status.

An approved HDE authorizes marketing of the HUD for clinical use, however clinical use of the device is limited to the indication specified in the product labeling. Also, a HUD may only be used in facilities that have established a local institutional review board (IRB) to oversee the clinical introduction and use of the device within that institution. The labeling for a HUD must state that the device is a humanitarian use device and that, although the device is authorized for clinical use by Federal law, the effectiveness of the device for the specific clinical indication for which it is approved has not been demonstrated.

Note: Use of a HUD for an indication that is NOT specified in the respective product labeling must comply with the FDA's and IRB's provisions for the Emergency Use of Unapproved Drugs or Devices (Refer to section 2.4 and Appendix B of this Reference Manual).

Refer to the following website for more information on the HDE process:

<http://www.fda.gov/cdrh/ode/hdeinfo.html>

REQUIREMENTS FOR HUD SUBMISSION TO THE UNIVERSITY OF PITTSBURGH

1. Initial IRB Approval: The HUD and its proposed use within the UPMC HS must be reviewed and approved by a convened IRB committee. Submit 26 copies of the following:
 - a. The HUD manufacturer's product labeling, clinical brochure, and/or other pertinent manufacturer informational materials.
 - b. The FDA HDE approval letter.
 - c. Written notification from the UPMC HS Research Fiscal Review Committee that it has approved the HUD for clinical use.
 - d. Written statement(s) from the responsible UPMC HS physician specifying how (i.e., for what clinical indication(s), where, and by whom the HUD will be used within the UPMC HS environment. Note that this statement must specify that use of the HUD will be limited to the clinical indication(s) listed in the FDA-approved product labeling.
 - e. Clinical Consent Form – Note that the Commonwealth of Pennsylvania requires written informed consent for all invasive clinical procedures. Thus, there should be a consent form to address 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. The HUD clinical consent form should be generally modeled after other clinical consent forms for invasive procedures to include the following:
 - (1) A description of an HDE/HUD approval process; e.g.

"Your medical care will involve the use of (specify device), which has been approved by the U.S. Food and Drug Administration (FDA) as a Humanitarian Use Device (HUD). A HUD is a device used to diagnose or treat a disease or condition that affects fewer than 4000 individuals in the United States per year and for which no comparable device is available. The FDA approves the clinical use of a HUD based primarily on evidence that it does not pose a significant risk of injury to the patient and that the potential benefit of the device to the health of the patient outweighs the risks of its use. The FDA approval of a HUD is based on limited data documenting its effectiveness in humans. Its use does not involve research."
 - (2) A description of the HUD and how this device will be used in the clinical setting. Based on this description, it should be clear to the patient why s/he is a candidate for the use of this device.
 - (3) A discussion of possible risks, side effects, and/or adverse events associated with the HUD and its proposed clinical use.
 - (4) A discussion of the possible benefits associated with the clinical use of the HUD.

- (5) A discussion of any alternative treatments or procedures (if any) that the patient may wish to consider in lieu of clinical application of the HUD.
- (6) Voluntary Consent statement(s) with patient signature and date lines.
- (7) Physician Certification statement with physician signature and date lines.

Please refer to the attached Consent Form outline for additional guidance.

2. Continuation of IRB Approval: Renewal of IRB approval is required annually. Submit 26 copies of the following information:
 - a. A cover letter, signed by the responsible physician, requesting continuation of IRB approval of the HUD. The cover letter, signed by the responsible physician, requesting continuation of the IRB approval for the HUD. The cover letter should identify the HUD and describe how (i.e., for what clinical indication(s), where, and by whom it will be used within the UPMC HS environment.
 - b. A copy of the current FDA-approved product labeling for the HUD.
 - c. A copy of the current IRB approved consent document.
 - d. For each patient in whom the HUD has been used during the previous year provide a summary of:
 - (1) the clinical indication for the use of the HUD;
 - (2) any adverse events felt to be related or possibly related to the use of the HUD; and
 - (3) the clinical outcome of the use of the HUD.
3. Manufacturer Modifications to the Humanitarian Use Device or Device Labeling (i.e., subsequent to FDA approval of additional clinical indications for use of the Humanitarian Use Device): IRB approval is required for any modifications of the device and/or proposed clinical use of the device. Submit 2 copies of the following information:
 - a. A cover letter, signed by the responsible physician, describing the modifications to the device and/or the proposed clinical use of the device and the rationale for such modification(s).
 - b. A copy of the HUD manufacturer's amendments to the HUD product labeling, clinical brochure, and/or other pertinent manufacturer informational materials corresponding to the requested modification(s).
 - c. A copy of the revised clinical use statement (see 1.d., above) and clinical consent form with the modifications highlighted.

4. Off-Label Use of a Humanitarian Use Device in Emergency or Compassionate Situations: 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 given patient. Under either of these situations, the involved physician and manufacturer of the device should, on a case-by-case:
- a. Notify the IRB Chair or Vice-Chair (physician) of the planned "off-label" use of the HUD. (The IRB Chair or Vice-Chair (physician) will provide an independent assessment as to whether the proposed use constitutes an emergency or compassionate situation.)
 - b. Obtain clinical informed consent for the "off-label" use of the HUD from the involved patient or his/her authorized representative (see example HUD clinical consent form).
 - c. Obtain approval of the UPMC HS Fiscal Review Committee for the proposed "off-label" use of the HUD.
 - d. Obtain authorization for the proposed "off-label" use of the HUD from the device manufacturer (i.e., the HDE holder).

In addition to the above measures, FDA approval for "off-label" use of the HUD should be obtained by the device manufacturer (i.e., the HDE holder) prior to the device for the emergency/compassionate use procedure.

**SAMPLE CONSENT DOCUMENT
HUMANITARIAN DEVICE EXEMPTIONS (HDE)**

(Division, Department or School Letterhead)

IRB Number

CLINICAL CONSENT FOR USE OF A HUMANITARIAN USE DEVICE

TITLE: Humanitarian Use Device: [Add Device Name]

HDE #: [Include #]

PRIMARY PHYSICIAN: Name
 Department
 Address
 Telephone Number with Area Code

SECONDARY PHYSICIAN: Names of all secondary physicians authorized to use the device
 Department
 Address
 Telephone Number with Area Code

What is a Humanitarian Use Device?

"Your medical care will involve the use of (specify device), which has been approved by the U.S. Food and Drug Administration (FDA) as a Humanitarian Use Device (HUD). A Humanitarian Use Device is a device used to diagnose or treat a disease or condition that affects fewer than 4,000 individuals in the United States per year and for which no comparable device is available. The U.S. Food and Drug Administration (FDA) approves the use of Humanitarian Use Devices based primarily on evidence that it does not pose a significant risk of injury to the patient and that the potential benefit of the device is to the health of the patient outweighs the risks of its use. Note that the use of the Humanitarian Use Device, "[name of device]" for [name of disease or condition] is approved by the FDA. The use of [name of device] will be limited to the indication listed in the protocol labeling by the FDA. Its use does not involve research."

[Insert a paragraph addressing a description of the Humanitarian Use Device and how it will be used.]

What will be involved with the use of this device?

"During your surgical procedure your physician would like to use the Humanitarian Use Device [name of device], to aid in the repair of your [state the disease or indication for use]. Your doctor has told you that you have [name the disease or condition] and because of this s/he would like to use the Humanitarian Use Device."

What are the possible risks, side effects and discomforts associated with the use of this device?

"Based on the results of the prior research studies on this device and experience with its approved use, the possibility of adverse events or side effects from the [name of the device] are the following:"

Provide quantitative information (using percentages AND number of people out of 100) on the frequency of possible adverse events. Use the following categories: Likely – occurs in more than 25% of people (more than 25 out of 100 people); Common – occurs in 1% to 25% of people (1 to 25 out of 100 people); Rare- occurs in less than 1% of people (less than 1 out of 100 people). In addition, we suggest that the risks are listed within the three categories in order of severity (i.e., death would be listed before hives). (Refer to the IRB Reference Manual, Chapter 7, Section 7.3; 4.4).

"There may be adverse events or side effects that are currently unknown and it is possible that certain of these unknown risks could be permanent, serious or life-threatening."

What are the possible benefits associated with the use of this device?

"It is felt that the use of this *[name of device]* during your *[add name of the procedure]* may benefit you in terms of *[list all benefits of the device]*."

What alternative treatments or procedures are available?

"If you decide not to take part in this treatment protocol, you may choose to have *[add list of alternatives]*."

Will my insurance provider or I be charged for the costs of this device or any procedure associated with its clinical use?

"You or your insurance provider will be responsible for any costs or charged associated with the use of the *[add the name of the device]* and the surgical procedures needed to insert the device. All other costs relating to your normal care will be billed in the usual manner."

VOLUNTARY CONSENT

"All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this treatment protocol and the physicians listed on the first page of this form will answer future questions."

Patient's signature

Date

PHYSICIAN'S CERTIFICATION

I certify that the nature and purpose, the potential benefits and possible risks associated with the *[name of device]* and its proposed clinical use have been explained to the above individual and that any questions about this information have been answered.

Physician's Signature

Date