Community Healthcare System
Central Institutional Review Board
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# Humanitarian Use Devices (HUD) FAQs For Physician/Investigators

## Definitions

### What is a Humanitarian Use Device (HUD)?

A Humanitarian Use Device (HUD) is defined in the Federal Food, Drug, and Cosmetic Act as a device that is "intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals per year in the United States."

HUD labeling information generally states that the device is a humanitarian use device for which effectiveness for the on label indication has not been demonstrated.

### What is a Humanitarian Device Exemption (HDE)?

A Humanitarian Device Exemption (HDE) is the application a manufacturer submits to obtain FDA approval of a Humanitarian Use Device. While it is similar to the premarket approval (PMA) application which a device manufacturer submits for most devices, the HDE submission does not require the manufacturer to meet the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a HUD.

## HUDs in Clinical Practice

### Is use of a HUD according to the manufacturer's instructions and labeling considered research?

No, use by a physician of a HUD for the purpose for which it is marketed is not research. However, use of a HUD in accordance with its label (on label) is permitted in the course of medical care only after the use or "protocol" has been submitted to and authorized by the CHS CIRB.

### Who is responsible for ensuring that a HUD is not administered to or implanted in a patient prior to obtaining IRB approval at a health care facility?

The physician/investigator is responsible for obtaining IRB approval before the HUD is administered to or implanted in a patient. The manufacturer who is usually the Humanitarian Device Exemption (HDE) holder is responsible for ensuring that the HUD is only used in facilities having an IRB constituted and acting in accordance with CFR 21 Part 56. The HDE holder will also not ship the device to an institution or physician/investigator if they are not in possession of IRB approval. Records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing IRBs, as well as any other information required by a reviewing IRB or FDA must be maintained by the HDE holder and sent to FDA.

### How do the regulations affect the use of the HUD in my practice?

There are 3 scenarios that are governed by FDA regulations in which a HUD may be used; 1.) the indication (on label) it was approved for, 2.) off-label, emergency use, and 3.) off-label, non-emergency use. The regulations affect the documentation and approvals that are required for each scenario.

**Do I have to submit each individual "on label" use of a humanitarian use device (HUD) to the CHS CIRB for approval before use?**

No. The CHS CIRB does not review and approve each individual use of a HUD. As long as the use of the HUD is within the FDA approved indication, the IRB approval to use the device is sufficient. The CHS CIRB requires that each on label use of an HUD must be reported to the CHS CIRB office within 5 working days. The summary should include the date, indication for use, any adverse effects, patient outcome and any additional information stipulated in the original CHS CIRB approval.

**In an emergency situation, can a HUD be used "off label" (i.e., outside of its approved indications for use)?**

Yes. The FDA does permit a HUD to be used off label in an emergency situation, but they require that certain patient protection measures be followed before the use occurs. Because IRB review and approval is required before a HUD is used within its approved labeling, a HUD should not be used outside of its approved labeling without similar restrictions. That is, in an emergency situation, a HUD may be used off-label to save the life or protect the physical well-being of a patient, but the physician/investigator and manufacturer (the HDE holder) should follow the emergency use procedures governing such use of unapproved devices as described in the CHS CIRB Policy; IRB 12, Emergency Use of a Test Article (Compassionate/Humanitarian Use)

According to this policy, before the device is used, if possible, the physician should obtain the IRB chairperson's concurrence, informed consent from the patient or his/her legal representative, and an independent assessment by an uninvolved physician. In addition, authorization from the manufacturer would be needed before the emergency use of the HUD. After the emergency use occurs, the physician should submit a follow-up report on the patient's condition and information regarding the patient protection measures to the CHS CIRB and to the manufacturer within 5 working days. The manufacturer then has a requirement to submit this report to the FDA as an amendment to the HDE.

**What if the situation is not an emergency, but the physician determines that there is no other alternative device for the patient's condition? Can a HUD be used under this type of situation (i.e., compassionate use)?**

Yes, a HUD may be used for compassionate use. This is the third type of "use" as described above, i.e., off label, non-emergent. In addition to addressing the patient protection measures, **prior** FDA approval of the HUD for compassionate use is required just as it is for compassionate use of any unapproved device. According to the FDA's policy on compassionate use, a physician who wishes to use a device for compassionate use should provide the HDE holder (manufacturer) with a description of the patient's condition and the circumstances necessitating treatment with the device, a discussion of why alternative therapies are unsatisfactory, and information to address the patient protection measures. For compassionate use of a HUD, the physician should provide this information to the manufacturer, who would then submit a HDE amendment for FDA approval before the use occurs. FDA will review the information in an expeditious manner and issue its decision to the HDE holder.

If the request is approved by FDA, the physician should devise an appropriate schedule for monitoring the patient, taking into consideration the limited information available regarding the potential risks and benefits of the device and the specific needs of the patient.

The physician must submit a request to the CHS CIRB for the compassionate (off label) use of the device with the manufacture's authorization, FDA authorization, and a written description for monitoring the patient following use. The CHS CIRB will expedite this request. The physician may not use the device until he as received concurrence from the CHS CIRB.

The physician must submit a report to the manufacturer and the CHS CIRB following use of the device reporting on the patient's outcome and progress.

**Is informed consent required when treating/diagnosing a patient with a HUD?**

Yes. Informing the patient is always required prior to initiating any treatment. Most HDE holders have developed patient labeling that incorporates information to assist a patient in making an informed decision about the use of the device. That is, 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. The CHS CIRB mandates use of this labeling information, along with the customary informed consent, for all HUD devices. An additional investigational informed consent is not required since the use of the HUD does not constitute research.

**What if the Manufacturer asks me to collect and provide them safety and effectiveness data to support a PMA? Is an IDE needed? Is IRB approval and informed consent required?**

This question really has several parts. If the manufacturer wants to collect safety and effectiveness data to support a PMA under their approved HDE, the health care provider can supply that information. But, if the HUD is the subject of a clinical investigation, (one in which safety and effectiveness data is being collected to support a Pre-Marketing Approval application), IRB approval and informed consent are required. (21 CFR Parts 56 and 50) Here, you should talk to the staff at the CHS CIRB office to insure that what the manufacturer is asking you to provide is in compliance with the FDA regulations.

## HUDs and the CHS CIRB

**If the HUD is marketed and approved by the FDA and its use is not research, why is the IRB involved?**

The IRB is involved for several reasons, all related to patient safety. The statute and the implementing regulation (see 21 CFR 814.124(a)) require IRB review and approval before a HUD is used. (There is an exception to this rule for emergency situations in which the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient.)

**What types of reviews must the CHS CIRB conduct with respect to HUDs?**

The IRB is responsible for initial as well as continuing review of the HUD. The initial review will be performed as a full board review. The CHS CIRB may elect to perform an expedited review for the continuing review. With respect to HUD review, the IRB will consider the ethical impact related to the use of the device and patient safety.

**How do I obtain CHS CIRB Approval?**

The IRB approval process for authorization to use HUDs within the Community Healthcare System is the same as required for research. The physician/investigator who will be responsible for the use of the HUD within the specific department prepares a submission package submitting his credentials/qualifications, identifying the device and its manufacturer, providing the HDE information for the device from the FDA, including the labeling information material which generally incorporates information to assist a patient in making an informed decision about the use of the device. That is, the patient labeling generally 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. The process differs from the submission process for research in that rather than identifying sub-investigators, the applying physician includes a list from the Medical Staff Credentialing Office of the institution of all those clinicians he will authorize to utilize the HUD under his direction, e.g., the roster of orthopedic surgeons

on a submission for a fixation device, etc. The physician/investigator attests to the fact that each of these physicians possesses the expertise necessary to use this device, are knowledgeable regarding the use of the device, and abide by the terms of the approval letter issued by the CHS CIRB.

**How long does it take to obtain approval from the CHS CIRB for a HUD?**

Depending when the submission was received, it will be placed on the agenda of the next convened meeting. The schedule of meeting dates and submission deadlines may be accessed on the Intranet or by contacting the CHS CIRB office.

**How long does the IRB approval last?**

The CHS CIRB must review any matter under its purview no less than once every 364 days. However, the CHS CIRB can direct that its continuing review should occur on a more frequent basis. The CHS CIRB will advise you in the approval letter when the next continuing review of the use of the HUD will occur.

**Once I obtain approval, what are my responsibilities?**

As a clinician your first responsibility is to secure at all times the safety and welfare of our patients. However, with regard to your IRB approval, as the submitting physician/investigator you are required to

1. Ensuring that all physician/investigators possess the credentials necessary to use the device, are knowledgeable regarding the use of the device and abide by the terms of the approval letter issued by the CHS CIRB.

2. Report on-label use of the HUD by any of the clinicians listed in the submission to the CHS CIRB office within 5 days.

3. In the event the HUD is proposed for use off-label or for a compassionate use, you should follow the guidance discussed above and make the CHS CIRB office aware of what action is proposed. Within 5 days following such off-label or compassionate use a full report of the events surrounding the decision, the procedure notes, the outcomes and a schedule for following up with the patient's condition should be provided to the office.

4. Report any serious adverse event related to the use of the HUD on your patient to the CHS CIRB office within 5 days.

5. Report any information regarding changes in labeling and potential patient risk received from the manufacturer or found by you in journals and other publications to the CHS CIRB office.

**What if there are changes to staff who I want to be able to use the HUD?**

If during the period of approval, there is a change in the list of clinicians approved by the Medical Staff Credentialing Office at your institution, you should submit an Amendment Request on an Abbreviated Submission Form to the CHS CIRB indicating which clinicians are no longer authorized and/or those additional clinicians who you agree to be responsible for in their use of the HUD. This will generally be handled under the expedited procedure process by the CHS CIRB. However, until the office issues an approval letter about the Amendment, those additional clinicians may not utilize the HUD at your institution.

**What does Continuing Review by the CHS CIRB mean?**

Continuing review means that the CHS CIRB considers all ethical and patient safety issues related to the subject matter of the submission as though it were looking at it for the first time. In the case of an HUD

submission, this would include review of the usage of the device during the prior period, the number of serious adverse events, if any, related to this use at the facility, system-wide, and world-wide and their effect on patients and patient safety, and any changes made by the manufacturer either to the device or the patient instructions since the last review by the IRB.

**How do I submit a Continuing Review to the CHS CIRB?**

Utilizing the Continuing Review forms available from the Office of Research Integrity, the submission for Continuing Review should basically track the initial submission indicating the usage of the device during the prior period, the number of serious adverse events, if any, related to this use at the facility, system-wide, and world-wide and their effect on patients and patient safety, and any changes made by the manufacturer either to the device or the patient instructions since it was last reviewed.

**Who do I contact if I have additional questions?**

The CHS CIRB has a direct line at Community Hospital; 219-836-6862 or email at; jlacera@comhs.org.

All policies and forms can be accessed on the CHS Intranet

You may also want to check the FDA web site http://www.fda.gov/ for additional information.

Of interest if you have specific questions you might look at http://www.fda.gov/orphan/HUDS/hudtips.html for information on submitting a Humanitarian Device Exemption request, http://www.fda.gov/orphan/humuse.htm for the FDA Guidance document authorizing the HUD program, and http://www.fda.gov/cdrh/ode/guidance/1381.html for the FDA Human Device Exemptions FAQ.

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