Yale University Institutional Review Boards

IRB Policy 610 The Use of Humanitarian Use Devices (HUDs) in Humans

Responsible Office	Office of Research Administration	Effective Date:	December 1, 2009
Responsible Official	Institutional Review Board Executive Chair	Last Revision:	March 7, 2013

Scope

This policy applies to clinicians initiating the clinical use of a device determined by the Food and Drug Administration (FDA) to be a Humanitarian Use Device (HUD) at Yale University School of Medicine or Yale-New Haven Hospital (YNHH). Note that HUD use by Yale investigators at the West Haven Veteran's Administration (VA) is governed by VA policy.

Policy Statement

In accordance with federal Food and Drug Administration (FDA) requirements (21 CFR §814.124(a) and Yale University policy, the Institutional Review Board (IRB) must approve the use of all Humanitarian Use Devices (HUDs) to be administered to, or implanted in, a patient at Yale University and/or Yale New Haven Hospital as set forth in this policy.

However, in the case of protocols to be carried out at YNHH, once approved by the IRB, the Principal Investigator must bring evidence of HUD approval and accompanying information or protocol to the relevant Human Protections Administrator at YNHH for approval insofar as inventory and costs may affect Hospital finances and procedures. Once approved by the relevant YNHH personnel, the Principal Investigator is responsible for undertaking the same process upon annual reapproval by the IRB.

Reason for the Policy

The FDA mandates that an Institutional Review Board (IRB) oversee the use of all HUDs in the course of medical practice. The FDA defines a HUD as "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 indiviudals in the United States per year." This means the FDA agrees that the device may benefit patients with a specific, rare, disease or condition. Because research has shown a HUD to have only "probable benefit", rather than a standard device trial which determines safety and effectiveness which is a higher mark than probable benefit, every HUD requires IRB approval and oversight, whether for use in clinical care or research.

HUDs represent one of the FDA's *compassionate* responses to the needs of the *few* rather than the needs of the *many*. In most instances, the device's manufacturer holds the Humanitarian Device Exemption (HDE) or Investigational Device Exemption from the FDA in order to market such devices. The sponsor (whether physician/investigator, manufacturer, or other party) holds an IDE to conduct clinical research aimed to determine the appropriateness of the device for a new indication.

The use of an HUD in accordance with the terms of the approved HDE and labeling for the HUD is not considered in and of itself to be "research" as defined by the FDA. Rather, use of the HUD would be a clinical use of an approved device. The use of an HUD at an institution must be approved by the institution's IRB, per FDA requirements.

In addition to its clinical use, an HDE holder may collect patient safety and effectiveness data for the HDE-approved indication(s) to support a premarket approval (PMA) application to the FDA. While this is a clinical investigation, FDA considers the investigation exempt from the requirement to obtain an Investigational Device Exemption (IDE), as the HUD is being used in accordance with the approved indication(s) described in labeling. The HUD as such is legally marketed and can be lawfully shipped without an IDE. IRB approval and patient consent to the procedure are still required, however, because they are FDA-regulated clinical investigations. However, manufacturers of the device can charge patients for HUDs under an HDE.

Definitions

Compassionate Use of a Humanitarian Use Device (HUD)
The use of an HUD in a situation that is not an emergency, but one for which a clinician determines there is no alternative device to treat the patient's condition. The FDA recommends that clinicians first obtain FDA approval for compassionate use.

Humanitarian Device Exemption (HDE)
FDA approval of a Humanitarian Device Exemption (HDE) application is necessary in order to allow the marketed use of a Humanitarian Use Device (HUD). The HDE is similar to a Pre-Market Approval (PMA), but because a HUD 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 HDE must contain sufficient information for FDA to determine that the probable benefit to health outweighs the risk of injury or illnesses, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

Humanitarian Use Device (HUD)
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. HUDs can only be used in a facility after an IRB has approved their use in that facility, except in certain emergencies.

Pre-Market Approval (PMA)
The FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices (See http://www.fda.gov/cdrh/devadvice/3132.html#class_3 for Class III device information).

Policy Sections

610.1 IRB Review of HUD Use
For an HUD to be used in treatment, diagnosis or research at Yale University or Yale-New Haven Hospital, the IRB and the FDA must approve the use, and the FDA must issue an HDE for the device to be permitted for use in humans. IRB approval of the use of an HUD cannot exceed the scope of the FDA approved indication(s). However, the Yale IRB reserves the right to limit the scope of the FDA approved indication, or impose any additional requirements for its use, as seen fit. The Yale IRB does not require review of each individual use of an HUD as long as the use of the HUD is consistent with the FDA-approved indication, and individual uses of the HUD are consistent with any limitations on its use put in place by the IRB. Once the IRB has approved the HUD, the PI is to submit the approval to the relevant YNHH Vice President or Service Line director for YNHH review and approval. If the HUD is approved for use at YNHH, an individual shall be designated in the relevant department to control the inventory, dispensation and chain of custody of the device(s). This individual must be notified of any use by the PI, prior to use for a planned procedure and as soon as possible thereafter in the event of an emergency use.

Clinicians are advised that the clinical investigation of an HUD beyond its approved indication(s) (e.g., for a broader or different indication) must be conducted in compliance with requirements for an IDE if the device is Significant Risk (See IRB Policy 600, Use of Investigational New Drugs and Devices in Humans).

The use of an HUD must initially be reviewed and approved by a fully convened IRB. The IRB may decide to use expedited review procedures for subsequent and continuing reviews since the initial review would have been performed by the full board, and use of the HUD within its approved labeling does not constitute research, according to FDA guidance. The fully convened IRB will determine at initial review whether or not subsequent and continuing reviews of the use of the HUD may be expedited in the future, provided no unanticipated problems have occurred with its use. Continuing review must be completed at least annually unless the IRB requires a shorter time frame.

610.2 Requirements of Clinicians
There must be a physician or healthcare provider listed as the principal responsible clinician for use of the device on the HUD application (located at http://info.med.yale.edu/hic/forms/index.html) submitted to the IRB. The application must be submitted prior to the use of the device except in an emergency, as addressed below. All other clinicians or healthcare providers who have the appropriate privileges and credentials and intend to administer the HUD as approved for use must also be listed on the HUD application.

The IRB requires that patients be informed of the use of an HUD by the utilization of either a patient consent document, an information sheet, patient brochure, or the device labeling. A discussion of the potential risks and benefits of the HUD, as well as any procedures associated with the use of the device, should be included in this

information, as well as the statement that the device is a humanitarian use device for which effectiveness for the labeled indication has not been demonstrated. The manufacturer's brochure will suffice when no safety and efficacy data will be collected.

610.3 Emergency Use of an HUD

If an emergency situation arises in which approval from the IRB cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior approval by the IRB. In such an emergency situation, an HUD may be used off-label to save the life or protect the physical well-being of a patient; however, in this situation, FDA recommends that the clinician and HDE holder follow the same emergency use procedures that govern the use of unapproved devices (See Policy 600, Use of Investigational New Drugs and Devices in Human Research). For example, before the device is used, if possible, the clinician should obtain the IRB chairperson's concurrence, consent to the procedure from the patient or his/her legal representative/surrogate, an independent assessment by an uninvolved (i.e., not the referring) physician, and institutional (YNHH) clearance. In addition, the clinician should obtain authorization from the HDE holder before the emergency use of the HUD. After the emergency use occurs, the clinician should submit a follow-up report on the patient's condition and information regarding the patient protection measures to the HDE holder, who would then submit this information as a HDE report to the FDA. This information should also be submitted to the Yale IRB for review **within 5 working days. The relevant departmental designee at YNHH must also be informed of the use and inventory adjusted appropriately thereafter.**

610.4 Compassionate Use of an HUD

As in the case of emergency use, FDA recommends and the Yale IRBs require that the clinician ensure that patient protection measures discussed above are addressed before the device is used. In addition, FDA approval for compassionate use should be sought before such use is undertaken. (See FDA Guidance on IDE Policies and Procedures http://www.fda.gov/cdrh/ode/idepolcy.html for more information.)

A clinician who wishes to use an 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.

610.5 Reporting Requirements of Clinicians

The number of HUD uses that fall within FDA-approved indication(s) and IRB limitation(s) (if applicable) must be reported by the physician/scientist to the IRB when requesting continuing review. All FDA actions and any changes to the FDA-approved indication for the use of the HUD must be reported to the IRB by the clinician or healthcare provider who requested use of the HUD as soon as possible, but no later than 5 working days after receiving knowledge of such actions or changes. Related correspondence from the HUD manufacturer (e.g., amended product labeling, clinical brochure, and patient brochure) or FDA (e.g., HDE amendment or supplement approval letters) must be submitted to the IRB.

Whenever a clinician or healthcare provider receives or otherwise becomes aware of information that reasonably suggests that a device with an approved HDE under his/her use: (1) may have caused or contributed to a death or serious injury; or (2) has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur, the physician or healthcare provider must report these findings to the FDA and IRB as soon as practicable but no more than 10 work days after the day that the physician or healthcare provider becomes aware of information.

The physician or healthcare provider must report any FDA action(s) regarding the HUD to the IRB promptly.

All changes to the HUD or the clinical use of the HUD must be reported to the IRB promptly.

Related Information.

IRB Policy 600: Use of Investigational New Drugs and Devices in Human Research

610 FR 1: Humanitarian Use Device Application

FDA Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors Frequently Asked Questions About Medical Devices, January 2006 (http://www.fda.gov/oc/gcp/guidance.html)

Guidance for Industry and FDA Staff - Humanitarian Device Exemption (HDE) Regulation: Questions and Answers, July 18, 2006.

Contacts

Subject	Contact	Phone
Humanitarian Use Devices	Human Investigation Committee	203-785-4688
Humanitarian Use Devices at Yale New Haven Hospital (YNHH)	Human Protections Administrator (HPA) at YNHH	203-688-2291

Roles and Responsibilities

Human Investigation Committee

HIC I, HIC II, HIC III and HIC IV serve as the four Institutional Review Boards or IRBs for biomedical human subjects research conducted at Yale University.

Human Protections Administrator at YNHH

Responsible for oversight and day-to-day management of human research protection at YNHH. Ensures that YNHH policies, procedures and practices are compliant with Yale policies, federal regulation and state laws.

Revision History

3/7/2013